L Number	Hits	Search Text	DB	Time stamp
1	9710	ligand-binding or ligand ADJ binding	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 10:36
7	2197	nf-KB OR RELA or p65	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 10:36
13	10	(ligand-binding or ligand ADJ binding) same (nf-KB OR RELA or p65)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:39
19	16	toniatti$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:39
25	0	toniatti$.in. and (nf-KB OR RELA or p65)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:40
31	0	toniatti$.in. and (ligand-binding or ligand ADJ binding)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:40
37	2	toniatti$.in. and regulation	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:41
43	181	siamak$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:42
49	0	siamak$.in. and (ligand-binding or ligand ADJ binding)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:43
55	0	siamak$.in. and (nf-KB OR RELA or p65)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:43
61	2	siamak$.in. and gene ADJ expression	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:50
67	182595	michael$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:51
73	11	siamak$.in. and michael$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:52
82	0	"wo 2002028168"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:53
88	2	"028168"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:54

94	0	"60/237633"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:54
100	0	"60/237,633"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:54
106	95	"28168"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:54
112	0	lotze$in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 11:55
-	660	nf-KB	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 10:35
-	1568	nf-KB OR RELA	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/05 10:36
-	746	P65	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:42
-	92	(nf-KB OR RELA) SAME P65	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:43
-	42562	TRANSCRIPTION	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:43
-	767810	FACTOR	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:43
-	136486	CHIMERIC OR FUSION	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:43
-	4	(nf-KB OR RELA) SAME P65 SAME TRANSCRIPTION SAME FACTOR SAME (CHIMERIC OR FUSION)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:54
-	393	HUMAN ADJ HEAT ADJ SHOCK ADJ FACTOR OR HSF	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:50
-	2	(HUMAN ADJ HEAT ADJ SHOCK ADJ FACTOR OR HSF) SAME P65 SAME TRANSCRIPTION SAME FACTOR SAME (CHIMERIC OR FUSION)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:53
-	923467	HOST ADJ CELL OR CELL	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:54

-	2	(nf-KB OR RELA) SAME P65 SAME TRANSCRIPTION SAME FACTOR SAME (CHIMERIC OR FUSION) SAME (HOST ADJ CELL OR CELL)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/03 16:56

L9 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 1999186585 MEDLINE
DOCUMENT NUMBER: 99186585 PubMed ID: 10088724
TITLE: Regulatory domain of human heat shock transcription factor-2 is not regulated by hemin or heat shock.
AUTHOR: Zhu Z; Mivechi N F
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Department of Radiology, Medical College of Georgia, Augusta 30912, USA.
CONTRACT NUMBER: CA62130 (NCI)
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (1999 Apr 1) 73 (1) 56-69.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990527

AB Heat shock **transcription factor** 2 (HSF-2) activates **transcription** of heat shock proteins in response to hemin in the human erythroleukemia cell line, K562. To understand the regulation of HSF-2 activation, a series of deletion mutants of HSF-2 fused to the GAL-4 DNA binding domain were generated. We have found that **human HSF**-2 has a regulatory domain located in the carboxyl-terminal portion of the protein which represses the activity of its activation domain under normal physiological conditions. The repressive effects of this domain can be eliminated by its deletion in GAL4-HSF-2 fusion constructs. The regulatory domain of HSF-2 can also repress a heterologous **chimeric** activator that contains a portion of the VP16 activation domain. The activation domain of HSF-2 is a segment of approximately 77 amino acids located proximal to the carboxyl-terminal hydrophobic heptad repeat (leucine zipper 4) of the molecule. Interestingly, the GAL4-HSF-2 fusion protein and the 77 amino acids activation domain are inactive and are not activated by pretreatment of cells with either hemin or elevated temperature. Our data suggest that regulation of HSF-2 differs from HSF-1 in that its regulatory domain is not responsive to hemin or heat directly.

L9 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 1998411354 MEDLINE
DOCUMENT NUMBER: 98411354 PubMed ID: 9738016
TITLE: Heat shock factor 1 mediates hemin-induced hsp70 gene transcription in K562 erythroleukemia cells.
AUTHOR: Yoshima T; Yura T; Yanagi H
CORPORATE SOURCE: HSP Research Institute, Kyoto Research Park, Shimogyo-ku, Kyoto 600-8813, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 25) 273 (39) 25466-71.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981021
Last Updated on STN: 19981021
Entered Medline: 19981015

AB Transcriptional induction of the hsp70 gene is mediated by **heat shock factor** 1 (HSF1) rapidly activated upon heat and other stresses. HSF2 has been thought to be responsible for accumulation of HSP70 during hemin-induced differentiation of human K562 erythroleukemia cells because of accompanying acquisition of HSF2 DNA

binding activity. However, there has not been any direct evidence for such a functional role of HSF2. The purpose of this study is to clarify the roles of HSF1 and HSF2 in HSP70 induction in hemin-treated K562 cells. We show here that a **chimeric** polypeptide of HSF2 and GAL4 DNA binding domain (GAL4-BD-HSF2) was unable to induce a GAL4 binding site-containing luciferase reporter gene in response to hemin and that exogenously overproduced HSF2 also failed to increase expression of a heat shock element-containing reporter. On the contrary, expression of a GAL4-BD-HSF1 **chimeric** protein responded to hemin treatment as well as to heat shock, and transiently overexpressed HSF1 caused hemin-responsive induction of the reporter gene in a dose-dependent manner. These results indicate that HSF1, rather than HSF2, primarily mediates the hemin-induced **transcription** of the hsp70 gene.

L9 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 1998028695 MEDLINE
DOCUMENT NUMBER: 98028695 PubMed ID: 9359875
TITLE: HSF1 granules: a novel stress-induced nuclear compartment of human cells.
AUTHOR: Cotto J; Fox S; Morimoto R
CORPORATE SOURCE: Department of Biochemistry, Rice Institute for Biomedical Research, Northwestern University, Evanston, IL 60208, USA.
SOURCE: JOURNAL OF CELL SCIENCE, (1997 Dec) 110 (Pt 23) 2925-34. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19990129
Entered Medline: 19980205

AB **Heat shock factor** 1 (HSF1) is the ubiquitous stress-responsive transcriptional activator which is essential for the inducible **transcription** of genes encoding heat shock proteins and molecular chaperones. HSF1 localizes within the nucleus of cells exposed to heat shock, heavy metals, and amino acid analogues, to form large, irregularly shaped, brightly staining granules which are not detected during attenuation of the heat shock response or when cells are returned to their normal growth conditions. The kinetics of detection of HSF1 granules parallels the transient induction of heat shock gene **transcription**. HSF1 granules are also detected using an HSF1-Flag epitope tagged protein or a **chimeric** HSF1-green fluorescent protein which reveals that these nuclear structures are stress-induced and can be detected in living cells. The spatial organization of HSF1 granules in nuclei of stressed cells reveals that they are novel nuclear structures which are stress-dependent and provides evidence that the nucleus undergoes dynamic reorganization in response to stress.

L9 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 96182086 MEDLINE
DOCUMENT NUMBER: 96182086 PubMed ID: 8622685
TITLE: The regulatory domain of human heat shock factor 1 is sufficient to sense heat stress.
AUTHOR: Newton E M; Knauf U; Green M; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 Mar) 16 (3) 839-46. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

> d 1-12

L13 ANSWER 1 OF 12 MEDLINE
AN 96430529 MEDLINE
DN 96430529 PubMed ID: 8833654
TI Angiotensinogen gene activation by angiotensin II is mediated by the rel A (nuclear factor-kappaB p65) transcription factor: one mechanism for the renin angiotensin system positive feedback loop in hepatocytes.
AU Li J; Brasier A R
CS Departments Internal Medicine and Sealy Center for Molecular Science, University of Texas Medical Branch, Galveston, USA.
NC 1R29-HL-45500 (NHLBI)
SO MOLECULAR ENDOCRINOLOGY, (1996 Mar) 10 (3) 252-64.
Journal code: 8801431. ISSN: 0888-8809.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970507
Last Updated on STN: 20000303
Entered Medline: 19970501

L13 ANSWER 2 OF 12 MEDLINE
AN 96405041 MEDLINE
DN 96405041 PubMed ID: 8809181
TI Generation of estrogen receptor mutants with altered ligand specificity for use in establishing a regulatable gene expression system.
AU Whelan J; Miller N
CS Glaxo Institute for Molecular Biology, Plan-Les-Ouates Geneva, Switzerland.
SO JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1996 Apr) 58 (1) 3-12.
Journal code: 9015483. ISSN: 0960-0760.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19970203
Entered Medline: 19961024

L13 ANSWER 3 OF 12 MEDLINE
AN 96189106 MEDLINE
DN 96189106 PubMed ID: 8628291
TI A glycine-rich region in NF-kappaB p105 functions as a processing signal for the generation of the p50 subunit.
AU Lin L; Ghosh S
CS Department of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute, New Haven, Connecticut 06520, USA.
NC R01-AI33443 (NIAID)
SO MOLECULAR AND CELLULAR BIOLOGY, (1996 May) 16 (5) 2248-54.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199606
ED Entered STN: 19960708
Last Updated on STN: 20000303
Entered Medline: 19960621

L13 ANSWER 4 OF 12 MEDLINE

AN 96182086 MEDLINE
DN 96182086 PubMed ID: 8622685
TI The regulatory domain of human heat shock factor 1 is sufficient to sense heat stress.
AU Newton E M; Knauf U; Green M; Kingston R E
CS Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
NC GM43901 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1996 Mar) 16 (3) 839-46.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199606
ED Entered STN: 19960627
Last Updated on STN: 19960627
Entered Medline: 19960618

L13 ANSWER 5 OF 12 MEDLINE
AN 96094309 MEDLINE
DN 96094309 PubMed ID: 7493948
TI Role of a distal enhancer containing a functional NF-kappa B-binding site in lipopolysaccharide-induced expression of a novel alpha 1-antitrypsin gene.
AU Ray A; Gao X; Ray B K
CS Department of Veterinary Pathobiology, University of Missouri, Columbia 65211, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Dec 8) 270 (49) 29201-8.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L42320
EM 199601
ED Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960111

L13 ANSWER 6 OF 12 MEDLINE
AN 95280936 MEDLINE
DN 95280936 PubMed ID: 7760831
TI A heat shock-responsive domain of human HSF1 that regulates transcription activation domain function.
AU Green M; Schuetz T J; Sullivan E K; Kingston R E
CS Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
NC GM43901 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1995 Jun) 15 (6) 3354-62.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950707
Last Updated on STN: 19970203
Entered Medline: 19950628

L13 ANSWER 7 OF 12 MEDLINE
AN 93180814 MEDLINE
DN 93180814 PubMed ID: 8441404
TI Conservation of transcriptional activation functions of the NF-kappa B p50

and p65 subunits in mammalian cells and Saccharomyces cerevisiae.
AU Moore P A; Ruben S M; Rosen C A
CS Roche Institute of Molecular Biology, Roche Research Center, Nutley, New Jersey 07110.
SO MOLECULAR AND CELLULAR BIOLOGY, (1993 Mar) 13 (3) 1666-74.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199304
ED Entered STN: 19930416
Last Updated on STN: 19930416
Entered Medline: 19930401

L13 ANSWER 8 OF 12 MEDLINE
AN 93054546 MEDLINE
DN 93054546 PubMed ID: 1331059
TI Tumor necrosis factor alpha and interferon gamma synergistically induce interleukin 8 production in a human gastric cancer cell line through acting concurrently on AP-1 and NF-kB-like binding sites of the interleukin 8 gene.
AU Yasumoto K; Okamoto S; Mukaida N; Murakami S; Mai M; Matsushima K
CS Department of Pharmacology, Kanazawa University, Japan.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31) 22506-11.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199212
ED Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921201

L13 ANSWER 9 OF 12 MEDLINE
AN 93024383 MEDLINE
DN 93024383 PubMed ID: 1406630
TI Selection of optimal kappa B/Rel DNA-binding motifs: interaction of both subunits of NF-kappa B with DNA is required for transcriptional activation.
AU Kunsch C; Ruben S M; Rosen C A
CS Department of Gene Regulation, Roche Institute of Molecular Biology, Nutley, New Jersey 07110.
SO MOLECULAR AND CELLULAR BIOLOGY, (1992 Oct) 12 (10) 4412-21.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
ED Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921026

L13 ANSWER 10 OF 12 MEDLINE
AN 92123171 MEDLINE
DN 92123171 PubMed ID: 1732726
TI Functional characterization of the NF-kappa B p65 transcriptional activator and an alternatively spliced derivative.
AU Ruben S M; Narayanan R; Klement J F; Chen C H; Rosen C A
CS Department of Gene Regulation, Roche Institute of Molecular Biology, Nutley, New Jersey 07110-1199.
SO MOLECULAR AND CELLULAR BIOLOGY, (1992 Feb) 12 (2) 444-54.

Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
ED Entered STN: 19920315
Last Updated on STN: 19920315
Entered Medline: 19920224

L13 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:438198 BIOSIS
DN PREV199699151804
TI Anatomy of TRAF2: Distinct domains for nuclear factor-kappa-B activation and association with tumor necrosis factor signaling proteins.
AU Takeuchi, Masahiro; Rothe, Mike; Goeddel, David V. (1)
CS (1) Tularik Inc., 2 Corporate Dr., South San Francisco, CA 94080 USA
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 33, pp. 19935-19942. ISSN: 0021-9258.
DT Article
LA English

L13 ANSWER 12 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 93343857 EMBASE
DN 1993343857
TI Heterologous C-terminal sequences disrupt transcriptional activation and oncogenesis by p59(v-rel).
AU Diehl J.A.; Hannink M.
CS Biochemistry Department, University of Missouri,Columbia, MO 65212, United States
SO Journal of Virology, (1993) 67/12 (7161-7171). ISSN: 0022-538X CODEN: JOVIAM
CY United States
DT Journal; Article
FS 004 Microbiology
LA English
SL English

=> d 1-12 ibib abs

L13 ANSWER 1 OF 12 MEDLINE
ACCESSION NUMBER: 96430529 MEDLINE
DOCUMENT NUMBER: 96430529 PubMed ID: 8833654
TITLE: Angiotensinogen gene activation by angiotensin II is mediated by the rel A (nuclear factor-kappaB p65) transcription factor: one mechanism for the renin angiotensin system positive feedback loop in hepatocytes.
AUTHOR: Li J; Brasier A R
CORPORATE SOURCE: Departments Internal Medicine and Sealy Center for Molecular Science, University of Texas Medical Branch, Galveston, USA.
CONTRACT NUMBER: 1R29-HL-45500 (NHLBI)
SOURCE: MOLECULAR ENDOCRINOLOGY, (1996 Mar) 10 (3) 252-64. Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 20000303
Entered Medline: 19970501
AB The renin-angiotensin system controls blood pressure through the enzymatic

production of the vasopressor angiotensin II (AII) from the angiotensinogen (AGT) precursor. Intravascular AII production stimulates de novo synthesis of its precursor in a positive feedback loop through increased gene expression. In this study, we investigate the effects of AII on AGT gene expression. At nanomolar concentrations, All activates **transcription** of the native AGT gene; this region is mapped to the AGT gene multihormone-inducible enhancer (-615 to -470). Within the multihormone-inducible enhancer, site-directed mutations of the acute-phase response element (APRE) that interfere with nuclear **factor**-kappa B (NF-kappa B) **transcription factor** binding also abolish All responsiveness. The APRE functions as a rapidly inducible All-inducible enhancer with peak reporter activity detected after a 4-h stimulation; this effect occurs only when the type 1 AII receptor is expressed. All induces sequence-specific **NF-KB** binding to the APRE in HepG2 nuclear extracts. Moreover, AII infusions of primary rat hepatocyte cultures produces a rapid 4-fold increase in sequence-specific NF-kappa B binding to the APRE. Antibodies against the transcriptional activator subunit, Rel A, quantitatively supershift the nucleoprotein complex, whereas antibodies to other NF-kappa B members do not, demonstrating that Rel A APRE-binding activity is AII-inducible. Transient overexpression of Rel A(1-551) activates the AGT multihormone-inducible enhancer. AII-inducible domains of Rel A were mapped by cotransfecting a **chimeric** GAL4-Rel A fusion protein with a reporter gene containing GAL4-binding sites. GAL4-Rel A(1-551) was an AII-inducible transactivator. Deletion of the NH(2)-terminal 254 amino acids of Rel A produces a constitutive transactivator, indicating that Rel A is activated by AII in a manner dependent on its NH(2) terminus. These studies define one mechanism for the renin-angiotensin system positive feedback loop in hepatocyctes.

L13 ANSWER 2 OF 12 MEDLINE
ACCESSION NUMBER: 96405041 MEDLINE
DOCUMENT NUMBER: 96405041 PubMed ID: 8809181
TITLE: Generation of estrogen receptor mutants with altered ligand specificity for use in establishing a regulatable gene expression system.
AUTHOR: Whelan J; Miller N
CORPORATE SOURCE: Glaxo Institute for Molecular Biology, Plan-Les-Ouates Geneva, Switzerland.
SOURCE: JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1996 Apr) 58 (1) 3-12.
Journal code: 9015483. ISSN: 0960-0760.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19970203
Entered Medline: 19961024

AB Considerable interest exists in developing an artificial system for the control of gene expression, based on the hormone binding domain (HBD) of steroid receptors. In this study we describe a yeast based approach which allows the identification of mutations within the HBD of steroid receptors, in this case the estrogen receptor, which result in altered specificity of the HBD with respect to its activation by ligands. Using this approach in yeast, we identified an estrogen receptor (HBD) mutant (His524 to Gln) whose activation by 17 beta-estradiol (E2) is significantly reduced while activation by a diphenol indene-ol compound (GR132706X) is increased, compared to the wild type estrogen receptor. When the activity of the mutant receptor was tested in mammalian cells the altered specificity was maintained. A **chimeric** **transcription factor** was constructed, in which the mutated estrogen receptor HBD was linked to the DNA binding domain of GAL4

and an 11 amino acid transcriptional activation domain of **RelA**. Reporter gene activation by this chimera was decreased in response to E2 and increased in response to GR132706X, as compared to the corresponding **chimeric transcription factor** containing the wild type estrogen receptor HBD. This approach should allow the development of a steroid receptor HBD based regulator of gene expression, whose activity is controlled specifically by a synthetic ligand, that would not affect the activity of endogenous steroid receptors.

L13 ANSWER 3 OF 12 MEDLINE
ACCESSION NUMBER: 96189106 MEDLINE
DOCUMENT NUMBER: 96189106 PubMed ID: 8628291
TITLE: A glycine-rich region in NF-kappaB p105 functions as a processing signal for the generation of the p50 subunit.
AUTHOR: Lin L; Ghosh S
CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute, New Haven, Connecticut 06520, USA.
CONTRACT NUMBER: R01-AI33443 (NIAID)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 May) 16 (5) 2248-54. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 20000303
Entered Medline: 19960621

AB **Transcription factor** NF-kappaB is generally considered to be a heterodimer with two subunits, p50 and **p65**. The p50 subunit has been suggested to be generated from its precursor, p105, via the ubiquitin-proteasome pathway. During processing, the C-terminal portion of p105 is rapidly degraded whereas the N-terminal portion (p50) is left intact. We report here that a 23-amino-acid, glycine-rich region (GRR) in p105 functions as a processing signal for the generation of p50. A GRR-dependent endoproteolytic cleavage downstream of the GRR releases p50 from p105, and this cleavage does not require any specific downstream sequences. p50 can be generated from **chimeric** precursor p105N-GRR-IkappaBalpha, while the C-terminal portion (IkappaBalpha) can also be recovered, suggesting that p105 processing includes two steps: a GRR-dependent endoproteolytic cleavage and the subsequent degradation of the C-terminal portion. We have also demonstrated that the GRR can direct a similar processing event when it is inserted into a protein unrelated to the NF-kappaB family and that it is therefore an independent signal for processing.

L13 ANSWER 4 OF 12 MEDLINE
ACCESSION NUMBER: 96182086 MEDLINE
DOCUMENT NUMBER: 96182086 PubMed ID: 8622685
TITLE: The regulatory domain of human heat shock factor 1 is sufficient to sense heat stress.
AUTHOR: Newton E M; Knauf U; Green M; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 Mar) 16 (3) 839-46. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960627

Last Updated on STN: 19960627
Entered Medline: 19960618

AB **Heat shock factor** (HSF) activates **transcription** in response to cellular stress. Human HSF1 has a central regulatory domain which can repress the activity of its activation domains at the control temperature and render them heat shock inducible. To determine whether the regulatory domain works in tandem with specific features of the HSF1 transcriptional activation domains, we first used deletion and point mutagenesis to define these activation domains. One of the activation domains can be reduced to just 20 amino acids. A GAL4 fusion protein containing the HSF 1 regulatory domain and this 20-amino-acid activation domain is repressed at the control temperature but potently activates **transcription** in response to heat shock. No specific amino acids in this activation domain are required for response to the regulatory domain; in particular, none of the potentially phosphorylated serine and threonine residues are required for heat induction, implying that heat-induced phosphorylation of the transcriptional activation domains is not required for induction. The regulatory domain is able to confer heat responsiveness to an otherwise completely heterologous **chimeric** activator that contains a portion of the VP16 activation domain, suggesting that the regulatory domain can sense heat in the absence of other portions of HSF1.

L13 ANSWER 5 OF 12 MEDLINE
ACCESSION NUMBER: 96094309 MEDLINE
DOCUMENT NUMBER: 96094309 PubMed ID: 7493948
TITLE: Role of a distal enhancer containing a functional NF-kappa B-binding site in lipopolysaccharide-induced expression of a novel alpha 1-antitrypsin gene.
AUTHOR: Ray A; Gao X; Ray B K
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Missouri, Columbia 65211, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Dec 8) 270 (49) 29201-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L42320
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960111

AB alpha 1-Antitrypsin (alpha 1-AT) is one of the major proteinase inhibitors in serum. Its primary physiological function is to inhibit neutrophil elastase activity in lung, but it also inhibits other serine proteases including trypsin, chymotrypsin, thrombin, and cathepsin. We have previously reported a novel alpha 1-AT, S-2 isoform, from rabbit that is induced up to 100-fold in the liver during acute inflammatory condition (Ray, B. K., Gao, X., and Ray, A. (1994) J. Biol. Chem. 269, 22080-22086). Here, we present evidence that the expression of this alpha 1-AT S-2 gene is also induced in lipopolysaccharide (LPS)-treated peripheral blood monocytes. From the cloned genomic DNA, we have identified a distal LPS-responsive enhancer located between -2438 and -1990 base pairs upstream of the **transcription** start site. In vitro DNA-binding studies demonstrated an interaction of an LPS-inducible NF-kappa B-like nuclear **factor** with a kappa B-element present in this enhancer region. Antibodies against **p65** and p50 subunits of NF-kappa B supershifted the DNA-protein complex. A mutation of the NF-kappa B-binding element virtually abolished the LPS-responsive induction of the **chimeric** promoter in monocytic cells. Furthermore, overexpression of NF-kappa B induced the wild-type promoter activity. Taken together, these results demonstrated that during LPS-mediated inflammation, NF-kappa

B/Rel family of **transcription factors** play a crucial role in the transcriptional induction of the inflammation responsive alpha 1-AT gene.

L13 ANSWER 6 OF 12 MEDLINE
ACCESSION NUMBER: 95280936 MEDLINE
DOCUMENT NUMBER: 95280936 PubMed ID: 7760831
TITLE: A heat shock-responsive domain of human HSF1 that regulates transcription activation domain function.
AUTHOR: Green M; Schuetz T J; Sullivan E K; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1995 Jun) 15 (6) 3354-62. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950707
Last Updated on STN: 19970203
Entered Medline: 19950628

AB **Human heat shock factor** 1 (HSF1) stimulates **transcription** from heat shock protein genes following stress. We have used **chimeric** proteins containing the GAL4 DNA binding domain to identify the transcriptional activation domains of HSF1 and a separate domain that is capable of regulating activation domain function. This regulatory domain conferred heat shock inducibility to **chimeric** proteins containing the activation domains. The regulatory domain is located between the transcriptional activation domains and the DNA binding domain of HSF1 and is conserved between mammalian and chicken HSF1 but is not found in HSF2 or HSF3. The regulatory domain was found to be functionally homologous between chicken and human HSF1. This domain does not affect DNA binding by the **chimeric** proteins and does not contain any of the sequences previously postulated to regulate DNA binding of HSF1. Thus, we suggest that activation of HSF1 by stress in humans is controlled by two regulatory mechanisms that separately confer heat shock-induced DNA binding and transcriptional stimulation.

L13 ANSWER 7 OF 12 MEDLINE
ACCESSION NUMBER: 93180814 MEDLINE
DOCUMENT NUMBER: 93180814 PubMed ID: 8441404
TITLE: Conservation of transcriptional activation functions of the NF-kappa B p50 and p65 subunits in mammalian cells and Saccharomyces cerevisiae.
AUTHOR: Moore P A; Ruben S M; Rosen C A
CORPORATE SOURCE: Roche Institute of Molecular Biology, Roche Research Center, Nutley, New Jersey 07110.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1993 Mar) 13 (3) 1666-74. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930416
Last Updated on STN: 19930416
Entered Medline: 19930401

AB The NF-kappa B **transcription factor** complex is composed of a 50-kDa (p50) and a 65-kDa (**p65**) subunit. Both subunits bind to similar DNA motifs and elicit transcriptional activation as either homo- or heterodimers. By using **chimeric** proteins that

contain the DNA binding domain of the yeast transcriptional activator GAL4 and subdomains of **p65**, three distinct transcriptional activation domains were identified. One domain was localized to a region of 42 amino acids containing a potential leucin zipper structure, consistent with earlier reports. Two other domains, both acidic and rich in prolines, were also identified. Of perhaps more significance, the same minimal activation domains that were functional in mammalian cells were also functional in the yeast Saccharomyces cerevisiae. Coexpression of the NF-kappa B inhibitory molecule, I kappa B, reduced the transcriptional activity of **p65** significantly, suggesting the ability of I kappa B to function in a similar manner in S. cerevisiae. Surprisingly, while the conserved rel homology domain of **p65** demonstrated no transcriptional activity in either mammalian cells or S. cerevisiae, the corresponding domain in p50 was a strong transcriptional activator in S. cerevisiae. The observation that similar domains elicit transcriptional activation in mammalian cells and S. cerevisiae demonstrates strong conservation of the transcriptional machinery required for NF-kappa B function and provides a powerful genetic system to study the transcriptional mechanisms of these proteins.

L13 ANSWER 8 OF 12 MEDLINE
ACCESSION NUMBER: 93054546 MEDLINE
DOCUMENT NUMBER: 93054546 PubMed ID: 1331059
TITLE: Tumor necrosis factor alpha and interferon gamma synergistically induce interleukin 8 production in a human gastric cancer cell line through acting concurrently on AP-1 and NF-kB-like binding sites of the interleukin 8 gene.
AUTHOR: Yasumoto K; Okamoto S; Mukaida N; Murakami S; Mai M; Matsushima K
CORPORATE SOURCE: Department of Pharmacology, Kanazawa University, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31) 22506-11.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921201

AB Interleukin 8 (IL-8) is a novel cytokine which possesses neutrophil chemotactic and activating activities in addition to chemotactic activity for basophils and T lymphocytes. It has been shown that IL-8 is produced by a variety of human somatic cells including monocytes/macrophages, dermal fibroblasts, vascular endothelial cells, keratinocytes, mesangeal cells, and several types of tumor cell lines. We have examined here whether or not human gastric cancer cell lines produce IL-8 in vitro. The production of IL-8 protein was detected by enzyme-linked immunosorbent assay in the culture supernatants derived from eight of nine human gastric cancer cell lines stimulated with either interleukin 1 alpha (IL-1 alpha), tumor necrosis **factor** alpha (TNF alpha), or TNF alpha plus interferon gamma (IFN gamma). In some of the gastric cancer cell lines such as MKN 45 and KATO, TNF alpha plus IFN gamma synergistically induced the production of IL-8. In MKN 45 cells, synergistic increase of the steady state level of IL-8 mRNA by TNF alpha plus IFN gamma was not inhibited by cycloheximide treatment. Scatchard analysis revealed that IFN gamma changed neither the number nor the affinity constant of TNF alpha binding sites on a gastric cancer cell line, suggesting that the synergism was a post-receptor event. Furthermore, synergistic induction of chloramphenicol acetyltransferase activity by TNF alpha plus IFN gamma was observed in MKN 45 that were transiently transfected with **chimeric** chloramphenicol acetyltransferase reporter genes driven by the

transcriptional regulatory region of human IL-8 gene. Through the mutation of the regulatory region of the IL-8 gene, both AP-1- and **NF-kB**-like **factor** binding elements were presumed to be involved in conferring the responsiveness to TNF alpha plus IFN gamma. Moreover, gel retardation analyses revealed that TNF alpha and IFN gamma synergistically induced the binding of **NF-kB** like as well as AP-1 like proteins bound to these sites. These results indicated that IFN gamma synergistically enhanced TNF alpha-induced IL-8 production in a human gastric cancer cell line through synergistic activation of **transcription factors** without up-regulating TNF alpha receptor.

L13 ANSWER 9 OF 12 MEDLINE
ACCESSION NUMBER: 93024383 MEDLINE
DOCUMENT NUMBER: 93024383 PubMed ID: 1406630
TITLE: Selection of optimal kappa B/Rel DNA-binding motifs: interaction of both subunits of NF-kappa B with DNA is required for transcriptional activation.
AUTHOR: Kunsch C; Ruben S M; Rosen C A
CORPORATE SOURCE: Department of Gene Regulation, Roche Institute of Molecular Biology, Nutley, New Jersey 07110.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1992 Oct) 12 (10) 4412-21. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921026

AB Analysis of the p50 and **p65** subunits of the NF-kappa B **transcription factor** complex has revealed that both proteins can interact with related DNA sequences through either homo- or heterodimer formation. In addition, the product of the proto-oncogene c-rel can bind to similar DNA motifs by itself or as a heterodimer with p50 or **p65**. However, these studies have used a limited number of known kappa B DNA motifs, and the question of the optimal DNA sequences preferred by each homodimer has not been addressed. Using purified recombinant p50, **p65**, and c-Rel proteins, optimal DNA-binding motifs were selected from a pool of random oligonucleotides. Alignment of the selected sequences allowed us to predict a consensus sequence for binding of the individual homodimeric Rel-related proteins, and DNA-protein binding analysis of the selected DNA sequences revealed sequence specificity of the proteins. Contrary to previous assumptions, we observed that **p65** homodimers can interact with a subset of DNA sequences not recognized by p50 homodimers. Differential binding affinities were also obtained with p50- and c-Rel-selected sequences. Using either a p50- or **p65**-selected kappa B motif, which displayed differential binding with respect to the other protein, little to no binding was observed with the heterodimeric NF-kappa B complex. Similarly, in transfection experiments in which the selective kappa B binding sites were used to drive the expression of a chloramphenicol acetyltransferase reporter construct, the **p65**- and p50-selected motifs were activated only in the presence of **p65** and p50/65 (a **chimeric** protein with the p50 DNA binding domain and **p65** activation domain) expression vectors, respectively, and neither demonstrated a significant response to stimuli that induce NF-kappa B activity. These findings demonstrate that interaction of both subunits of the heterodimeric NF-kappa B complex with DNA is required for DNA binding and transcriptional activation and suggest that transcriptional activation mediated by the individual rel-related proteins will differ dramatically, depending on the specific kappa B motifs present.

ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The tumor necrosis **factor** (TNF) receptor-associated **factor** (TRAF) family of proteins interact with and transduce signals for members of the TNF receptor superfamily. TRAF1, TRAF2, and TRAF3 share a conserved C-terminal TRAF domain. TRAF2 plays a key role in transducing signals for activation of the **transcription factor** nuclear **factor**-kappa-B (NF-kappa-B). We have performed extensive mutational analysis on TRAF2, examining the requirements for **NF-KB** activation, self-association, and interaction with other molecules involved in TNF signaling. Examination of point mutants and TRAF2-TRAF3 **chimeric** proteins indicates that the N-terminal RING finger and two adjacent zinc fingers of TRAF2 are required for NF-kappa-CB activation. The two distinct TRAF-N and TRAF-C subdomains of the TRAF domain appear to independently mediate self-association and interaction with TRAF1. Interaction of TRAF2 with TNF-R2 and TRADD requires sequences at the C terminus of the TRAF-C domain, whereas interaction with the protein kinase receptor-interacting protein V(RIP) occurs via sequences at the N terminus of the TRAF-C domain. Thus, distinct domains of TRAF2 are involved in recruitment and signaling functions.

L13 ANSWER 12 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93343857 EMBASE
DOCUMENT NUMBER: 1993343857
TITLE: Heterologous C-terminal sequences disrupt transcriptional activation and oncogenesis by p59(v-rel).
AUTHOR: Diehl J.A.; Hannink M.
CORPORATE SOURCE: Biochemistry Department, University of Missouri,Columbia, MO 65212, United States
SOURCE: Journal of Virology, (1993) 67/12 (7161-7171).
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Members of the **NF-kB**/rel family of **transcription factors** are regulated through a trans association with members of a family inhibitor proteins, collectively known as IkB proteins, that contain five to eight copies of a 33-amino-acid repeat sequence (ankyrin repeat). Certain **NF-kB**/rel proteins are also regulated by cis-acting ankyrin repeat-containing domains. The C terminus of p105(**NF-kB**), the precursor of the 50-kDa subunit of **NF-kB**, contains a series of ankyrin repeats; proteolytic removal of this ankyrin domain is necessary for the manifestation of sequence-specific DNA binding and nuclear translocation of the N-terminal product. To investigate the structural requirements important for regulation of different **NF-kB**/rel family members by polypeptides containing ankyrin repeat domains, we have constructed a p59(v-rel):p105(**NF-kB**) **chimeric** protein (p110(v-rel-ank)). The presence of C-terminal p105(**NF-kB**)-derived sequences in p110(v-rel-ank) inhibited nuclear translocation, sequence-specific DNA binding, PP40(IkB-.alpha.) association, and oncogenic transformation. Sequential truncation of the C- terminal ankyrin domain of p110(v-rel-ank) resulted in the restoration of nuclear translocation, DNA binding, and pp40(IkB-.alpha.) association but did not restore the oncogenic properties of p59(v-rel). The presence of 67 C-terminal p105(**NF-kB**)-derived amino acids was sufficient to inhibit both transcriptional activation and oncogenic transformation by p59(v-rel). These results support a model in which activation of gene expression by p59(v-rel) is required for its ability to induce oncogenic transformation.

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=> d his

     (FILE 'HOME' ENTERED AT 16:55:10 ON 03 SEP 2002)

     FILE 'MEDLINE' ENTERED AT 16:57:19 ON 03 SEP 2002
L1          1182 S NF-KB OR "RELA"
L2          3098 S NF-KB OR "RELA" OR P65
L3           346 S L1 AND P65
L4         18829 S CHIMERIC
L5        185303 S TRANSCRIPTION
L6       1842828 S FACTOR
L7             9 S L3 (S) L4 (S) L5 (S) L6
L8           692 S HUMAN HEAT SHOCK FACTOR OR HEAT SHOCK FACTOR OR HUMAN HSF
L9             5 S L8 (S) L4 (S) L5 (S) L6

     FILE 'MEDLINE, USPATFULL, PCTFULL, BIOSIS, EMBASE, CAPLUS, CONFSCI,
     SCISEARCH' ENTERED AT 17:06:13 ON 03 SEP 2002
L10           27 S L8 (S) L4 (S) L5 (S) L6
L11          119 S L2 (S) L4 (S) L5 (S) L6
L12           59 DUP REM L10 L11 (87 DUPLICATES REMOVED)
L13           12 S L12 NOT PY>1996

=> d l12 1-59 ibib abs

L12  ANSWER 1 OF 59  USPATFULL
ACCESSION NUMBER:         2002:202067  USPATFULL
TITLE:                    Compositions and methods for inducing gene expression
INVENTOR(S):              Gregory, Richard J., Westford, MA, United States
                          Vincent, Karen, Arlington, MA, United States
PATENT ASSIGNEE(S):       Genzyme Corporation, Cambridge, MA, United States (U.S.
                          corporation)

                               NUMBER        KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 6432927          B1   20020813
APPLICATION INFO.:        US 2000-579897           20000526  (9)
RELATED APPLN. INFO.:     Continuation-in-part of Ser. No. US 133612

                                 NUMBER         DATE
                          ------------------ --------
PRIORITY INFORMATION:     US 1997-67546P     19971204 (60)
DOCUMENT TYPE:            Utility
FILE SEGMENT:             GRANTED
PRIMARY EXAMINER:         Nguyen, Dave T.
LEGAL REPRESENTATIVE:     Kanter, Madge R.
NUMBER OF CLAIMS:         31
EXEMPLARY CLAIM:          1
NUMBER OF DRAWINGS:       8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT:               2175
AB      The present invention provides recombinant nucleic acid molecules
        encoding a chimeric transactivator protein including a DNA binding
        domain of a DNA binding protein and a protein domain capable of
        transcriptional activation. The present invention also provides
        recombinant viral and non-viral vectors that are able to infect and/or
        transfect and sustain expression of a biologically active chimeric
        transactivator proteins in mammalian cells. Also provided are host cell
        lines and non-human transgenic animals capable of expressing
        biologically active chimeric transactivator proteins. In another aspect,
        compositions and methods for treating or preventing ischemic damage
        associated with hypoxia-related disorders are provided.
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L12 ANSWER 2 OF 59 USPATFULL

ACCESSION NUMBER: 2002:199080 USPATFULL
TITLE: Regulation of biological events using novel compounds
INVENTOR(S): Clackson, Timothy P., Arlington, MA, UNITED STATES
Gilman, Michael Z., Newton, MA, UNITED STATES
Holt, Dennis A., Schwenksville, PA, UNITED STATES
Keenan, Terence P., Cambridge, MA, UNITED STATES
Rozamus, Leonard, Bedford, MA, UNITED STATES
Yang, Wu, Princeton, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002107189	A1	20020808
APPLICATION INFO.:	US 2001-781804	A1	20010212 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-12097, filed on 22 Jan 1998, GRANTED, Pat. No. US 6187757 Continuation-in-part of Ser. No. US 1997-791044, filed on 28 Jan 1997, ABANDONED Continuation-in-part of Ser. No. US 1995-481941, filed on 7 Jun 1995, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1996-US9948	19960607
	US 1996-15502P	19960209 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: David L. Berstein, ARIAD Pharmaceuticals, Inc., 26 Landsdowne Street, Cambridge, MA, 02139-4234
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 5858
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Materials and methods are disclosed for regulation of biological events such as target gene transcription and growth, proliferation or differentiation of engineered cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 59 USPATFULL

ACCESSION NUMBER: 2002:92274 USPATFULL
TITLE: Methods and materials for regulated production of proteins
INVENTOR(S): Natesan, Sridaran, Chestnut Hill, MA, UNITED STATES
Clackson, Timothy P., Cambridge, MA, UNITED STATES
Pollock, Roy M., Medford, MA, UNITED STATES
PATENT ASSIGNEE(S): ARIAD Gene Therapeutics, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002048792	A1	20020425
APPLICATION INFO.:	US 2001-906189	A1	20010716 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-488267, filed on 20 Jan 2000, ABANDONED Continuation-in-part of Ser. No. US 1998-140149, filed on 26 Aug 1998, GRANTED, Pat. No. US 6117680 Continuation-in-part of Ser. No. US 1998-126009, filed on 29 Jul 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-920610, filed on 27 Aug 1997, GRANTED, Pat. No. US 6015709 Continuation-in-part of Ser. No. US 1997-918401, filed on 26 Aug 1997, ABANDONED Continuation-in-part of Ser. No. WO 1997-US15219, filed on 27 Aug 1997, UNKNOWN
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: ARIAD Pharmaceuticals, Inc., 26 Landsdowne Street, Cambridge, MA, 02139
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 2116
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods and materials for regulated production of proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 59 USPATFULL
ACCESSION NUMBER: 2002:129786 USPATFULL
TITLE: Modulation of vascular cell adhesive molecule expression through oligonucleotide interactions
INVENTOR(S): Medford, Russell M., Atlanta, GA, United States
Bennett, Clarence Frank, Carlsbad, CA, United States
PATENT ASSIGNEE(S): ISIS Pharmaceuticals, Inc., Carlsbad, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6399376	B1	20020604	
APPLICATION INFO.:	US 1993-147878		19931105	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: McGarry, Sean
ASSISTANT EXAMINER: Epps, Janet L.
LEGAL REPRESENTATIVE: Woodcock Washburn LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1170
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Genes coding for vascular cell adhesion molecules, particularly VCAM-1, are modulated through interaction of oligonucleotides with transcriptional regulatory factors which bind to the genes. Specific and effective oligonucleotides are provided which interact with the transcriptional regulatory factors to diminish their interaction with the genes and downregulate their function. Multi-modal oligonucleotides are also provided which interact both with a transcriptional regulatory factor and with another aspect of gene function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 59 PCTFULL COPYRIGHT 2002 Univentio
ACCESSION NUMBER: 2002029068 PCTFULL ED 20020627 EW 200215
TITLE (ENGLISH): VECTOR SYSTEM FOR PLANTS
TITLE (FRENCH): SYSTEME VECTORIEL POUR PLANTES
INVENTOR(S): GLEBA, Yuri; DOROKOV, Yurii; IVANOV, Peter; ATABEKOV, Joseph
PATENT ASSIGNEE(S): ICON GENETICS AG, for all designates States except US; GLEBA, Yuri, for US only; DOROKOV, Yurii, for US only; IVANOV, Peter, for US only; ATABEKOV, Joseph, for US only
AGENT: WAeCHTERSHAeUSER, Guenter
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002029068	A2	20020411

DESIGNATED STATES AE AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ
DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW
MX NO NZ PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA
UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA
GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-EP11629 A 20011008
PRIORITY INFO.: DE 2000-100 49 587.7 20001006

ABEN The invention describes virus-based amplification vectors for plants containing additional plant-specific internal ribosome entry site (IRES) element(s) allowing for a polycistronic translation and a cap-independent translation of : a) heterologous gene(s); b) whole viral genome or c) viral subgenomic RNAs. Said IRES elements are of plant viral origin, or they are isolated from other organisms or engineered using different synthesis procedures. Said IRES element(s) and said heterologous gene(s) are inserted into ampification vectors and allow for the expression of said heterologous gene(s) in the absence of additional viral promoters, in particular, said expression is achieved through cap-independent translation.

ABFR L'invention concerne des vecteurs d'amplification a base de virus pour des plantes contenant un ou plusieurs sites d'entree internes des ribosomes (IRES) supplementaires specifiques aux plantes, permettant une traduction polycistronique et une traduction independante de la coiffe a) d'un ou de plusieurs genes, b) du genome viral complet ou c) des ARN viraux sous-genomiques. Ces elements IRES sont obtenus a partir de virus de plantes, isoles a partir d'autres organismes ou mis au point a l'aide de differents processus de synthese. Ces elements IRES et lesdits genes heterologues sont introduits dans des vecteurs d'amplification et permettent l'expression desdits genes heterologues en l'absence de promoteurs viraux supplementaires. Plus particulierement, ladite expression est obtenue par traduction independante de la coiffe.

L12 ANSWER 6 OF 59 PCTFULL
ACCESSION NUMBER: 2002016591 PCTFULL ED 20020711 EW 200209
TITLE (ENGLISH): 49937, 49931, AND 49933, NOVEL HUMAN TRANSPORTER FAMILY MEMBERS AND USES THEREOF
TITLE (FRENCH): 49937, 49931, ET 49933, NOUVEAUX ELEMENTS DE LA FAMILLE DES TRANSPORTEURS HUMAINS ET UTILISATION DE CES DERNIERS
INVENTOR(S): CURTIS, Rory, A., J.; CHUN, Miyoung
PATENT ASSIGNEE(S): MILLENNIUM PHARMACEUTICALS, INC., for all designates States except US; CURTIS, Rory, A., J., for US only; CHUN, Miyoung, for US only
AGENT: MANDRAGOURAS, Amy, E.
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002016591	A2	20020228

DESIGNATED STATES AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW
MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE
CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF
BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US26212 A 20010821
PRIORITY INFO.: US 2000-60/226,504 20000821
US 2000-60/250,932 20001130

ABEN The invention provides isolated nucleic acid molecules, designated HEAT nucleic acid molecules, which encode novel transporter family members. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing HEAT nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a HEAT gene has been introduced or disrupted. The invention still further provides isolated HEAT proteins, fusion proteins, antigenic peptides and anti-HEAT antibodies. Diagnostic and therapeutic methods utilizing compositions of the invention are also provided.

ABFR La presente invention concerne des molecules d'acide nucleique isolees, des molecules d'acide nucleique HEAT, qui codent de nouveaux membres de la famille des transporteurs. L'invention concerne des molecules d'acide nucleique antisens, des vecteurs d'expression de recombinaison contenant des molecules d'acide nucleique antisens contenant des molecules d'acide nucleique HEAT, des cellules hotes dans lesquelles on a introduit des vecteurs d'expression et des animaux transgeniques non humains dans lesquels un gene HEAT a ete introduit ou interrompu. L'invention concerne des proteines HEAT isolees, des proteines de fusion, des peptides antigenes, et des anticorps anti-HEAT. L'invention traite de procedes diagnostiques et therapeutiques utilisant des compositions selon l'invention.

L12 ANSWER 7 OF 59 PCTFULL COPYRIGHT 2002 Univentio

ACCESSION NUMBER:	2002046412 PCTFULL ED 20020624 EW 200224
TITLE (ENGLISH):	REGULATION OF ANGIOGENESIS WITH ZINC FINGER PROTEINS
TITLE (FRENCH):	REGULATION DE L'ANGIOGENESE AU MOYEN DE PROTEINES A DOIGTS DE ZINC
INVENTOR(S):	REBAR, Edward; JAMIESON, Andrew; LIU, Qiang; LIU, Pei-Qi; WOLFFE, Alan; EISENBERG, Stephen, P.; JARVIS, Eric
PATENT ASSIGNEE(S):	SANGAMO BIOSCIENCES, INC., for all designates States except US; REBAR, Edward, for US only; JAMIESON, Andrew, for US only; LIU, Qiang, for US only; LIU, Pei-Qi, for US only; WOLFFE, Alan, for US only; EISENBERG, Stephen, P., for US only; JARVIS, Eric, for US only
AGENT:	SERAFINI, Andrew, T.
LANGUAGE OF PUBL.:	English
LANGUAGE OF FILING:	English
DOCUMENT TYPE:	Patent
PATENT INFORMATION:	

NUMBER	KIND	DATE
WO 2002046412	A2	20020613

DESIGNATED STATES AE AG AL AM AT AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ CZ DE DE DK DK DM DZ EC EE EE ES FI FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 2001-US46861	A	20011206
PRIORITY INFO.:	US 2000-09/733,604		20001207
	US 2000-09/736,083		20001212
	US 2001-09/846,033		20010430

ABEN Provided herein are a variety of methods and compositions for regulating angiogenesis, such
methods and compositions being useful in a variety of applications where modulation
of vascular formation is useful, including, but not limited to, treatments for

ischemia and wound healing. Certain of the methods and compositions accomplish this by using various zinc finger proteins that bind to particular target sites in one or more VEGF genes. Nucleic acids encoding the zinc finger proteins are also disclosed. Methods for modulating the expression of one or more VEGF genes with the zinc finger proteins and nucleic acids are also disclosed. Such methods can also be utilized in a variety of therapeutic applications that involve the regulation of endothelial cell growth. Pharmaceutical compositions including the zinc finger proteins or nucleic acids encoding them are also provided.

ABFR L'invention concerne une variete de procedes et de compositions destines a reguler l'angiogenese, des procedes et des compositions s'averant utiles dans une variete d'applications dans lesquelles la modulation de formation vasculaire est utile, telles, qu'entre autres, les traitements de l'ischemie et ceux stimulant la cicatrisation. Pour ce faire, certains procedes et certaines compositions utilisent des proteines a doigts de zinc qui lient les sites cibles particuliers a un ou plusieurs genes du facteur de croissance endothelial vasculaire (VEGF). L'invention concerne egalement des acides nucleiques codant les proteines a doigts de zinc, et des procedes de modulation de l'expression d'un ou plusieurs genes du VEGF au moyen des proteines a doigts de zinc et des acides nucleiques. Ces procedes peuvent aussi etre utilises dans une variete d'applications therapeutiques impliquant la regulation de la croissance des cellules endotheliales. L'invention concerne enfin des compositions pharmaceutiques contenant des proteines a doigts de zinc ou des acides nucleiques les codant.

L12 ANSWER 8 OF 59 PCTFULL COPYRIGHT 2002 Univentio

ACCESSION NUMBER: 2002002765 PCTFULL ED 20020814

TITLE (ENGLISH): CHIMERIC PROMOTERS FOR CONTROLLING EXPRESSION IN SMOOTH MUSCLE CELLS

TITLE (FRENCH): PROMOTEURS CHIMERIQUES PERMETTANT DE COMMANDER L'EXPRESSION DANS LES CELLULES DES MUSCLES LISSES

INVENTOR(S): RIBAULT, Sebastien; NEUVILLE, Pascal; MEHTALI, Majid

PATENT ASSIGNEE(S): TRANSGENE S.A.; RIBAULT, Sebastien; NEUVILLE, Pascal; MEHTALI, Majid

DOCUMENT TYPE: Patent

PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2002002765	A2	20020110

DESIGNATED STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 2001-EP7657	A	20010704
PRIORITY INFO.:	EP 2000-00440208.7		20000705
	US 2000-60/246,084		20001107

ABEN The present invention concerns a chimeric construct comprising a SMC-specific promoter operably linked to a muscle-specific enhancer. It also provides an expression cassette comprising such a chimeric construct to control expression of a therapeutic gene. Finally, the

invention relates to a recombinant vector, a viral particle, an eukaryotic host cell, a composition comprising said expression cassette and their use for specific expression in SMCs and for therapeutic or prophylactic purposes, a method for the treatment of a human or animal organism as well as a transgenic non-human animal comprising integrated into its genome the chimeric construct, the expression cassette or the vector of the present invention.

ABFR La presente invention concerne un produit de recombinaison chimerique comprenant un promoteur specifique de la cellule du muscle lisse, lie de maniere operationnelle a un amplificateur specifique des muscles. L'invention traite egalement d'une cassette d'expression comprenant un produit de recombinaison chimerique de ce type pour commander l'expression d'un gene therapeutique. Enfin, l'invention concerne un vecteur de recombinaison, une particule virale, une cellule hote eucaryote, une composition comprenant ladite cassette d'expression et leur utilisation pour l'expression specifique dans les cellules des muscles lisses et les applications therapeutiques ou prophylactiques. L'invention traite d'un procede pour traiter un organisme humain ou animal ainsi qu'un animal non humain transgenique dans le genome duquel sont integres le produit de recombinaison chimerique, la cassette d'expression ou le vecteur selon l'invention.

L12 ANSWER 9 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:429055 CAPLUS
DOCUMENT NUMBER: 137:16544
TITLE: Human heparanase gene regulatory sequences and their use for regulation of heterologous genes
INVENTOR(S): Wolffe, Alan P.; Qi, Hong
PATENT ASSIGNEE(S): Sangamo Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044353	A2	20020606	WO 2001-US44798	20011130

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-250690P P 20001130

AB Nucleotide sequences comprising regulatory regions upstream and downstream of the coding region of the human heparanase gene are provided. Also provided are mols. which regulate gene expression through their interaction with heparanase regulatory sequences. These methods and compns. allow for targeted modulation of expression of the heparanase gene, as well as modulation of expression of a target gene using heparanase regulatory sequences. Compns. include functional domains fused to a DNA-binding domain specific for heparanase regulatory sequences, such as, for example, a designed zinc finger DNA-binding domain. Chimeric activator and repressor proteins bind to relevant target sites in the heparanase gene and activate or repress heparanase transcription.

L12 ANSWER 10 OF 59 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002150196 MEDLINE
DOCUMENT NUMBER: 21877102 PubMed ID: 11882633
TITLE: Hypoxia inducible double plasmid system for myocardial

ischemia gene therapy.
AUTHOR: Tang Yi; Jackson MaShira; Qian Keping; Phillips M Ian
CORPORATE SOURCE: Department of Physiology and Functional Genomics, University of Florida, Gainesville 32610, USA.
SOURCE: HYPERTENSION, (2002 Feb) 39 (2 Pt 2) 695-8. Journal code: 7906255. ISSN: 1524-4563.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020308
Last Updated on STN: 20020403
Entered Medline: 20020328

AB Coronary artery disease frequently involves repeated bouts of myocardial ischemia. To automatically up-regulate the cardioprotective transgenes under hypoxic ischemia, a "vigilant vector" gene therapy system was developed and tested in a rat embryonic myocardial cell line (H9c2). In the vigilant vector, a hypoxia response element-incorporated promoter was used as a switch to turn on the gene expression in response to hypoxic signal. Furthermore, a novel double plasmid system was designed to elevate the potency of the vigilant vector. Instead of putting the promoter and the reporter gene in the same plasmid (single plasmid system), we separated them into two plasmids: the transactivator plasmid and reporter plasmid (double plasmid system). The hypoxia response element (HRE)-incorporated promoter increased the expression of a **chimeric transcription factor** consisting of the yeast GAL4 DNA binding domain and the human nuclear (**transcription**) **factor**-kappaB (NF-kappaB) **p65** activation domain. The powerful **chimeric** regulator binds specifically to the upstream activating sequence for GAL4 in the reporter plasmid and activates the **transcription** of the transgene. Our experiments showed that the HRE-mediated expression could quickly increase 2.08 +/- 0.75-fold within 6 hours of hypoxia and further augmented 7.12 +/- 1.52-fold when the hypoxia condition was prolonged to 24 hours. The hypoxia-inducible double plasmid system dramatically amplified the transgene expression under both hypoxia and normoxia by 412.79 +/- 185.27-fold and 205.35 +/- 65.44-fold, respectively, relative to the single plasmid system. From these results, we concluded that this hypoxia inducible double plasmid system could be used therapeutically to switch on genes that have proven beneficial effects in myocardial ischemia.

L12 ANSWER 11 OF 59 USPATFULL DUPLICATE 2
ACCESSION NUMBER: 2001:185087 USPATFULL
TITLE: Heterologous transcription factors
INVENTOR(S): Gilman, Michael Z., Newton, MA, United States
Natesan, Sridaran, Chestnut Hill, MA, United States
PATENT ASSIGNEE(S): ARIAD Gene Therapeutics, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6306649	B1	20011023	
APPLICATION INFO.:	US 1996-672213		19960627	(8)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1995-553P	19950627	(60)
	US 1995-19614P	19951229	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Martin, Jill D.
LEGAL REPRESENTATIVE: Berstein, David L.
NUMBER OF CLAIMS: 2

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 2484
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides novel materials and methods involving the heterologous expression of transcription factors which are useful for effecting transcription of target genes in genetically engineered cells or organisms containing them. Target gene constructs and other materials useful for practicing the invention are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 12 OF 59 USPATFULL DUPLICATE 3
ACCESSION NUMBER: 2001:22203 USPATFULL
TITLE: Regulation of biological events using novel compounds
INVENTOR(S): Clackson, Timothy P., Cambridge, MA, United States
Gilman, Michael Z., Newton, MA, United States
Holt, Dennis A., Royersford, PA, United States
Keenan, Terence P., Cambridge, MA, United States
Rozamus, Leonard, Bedford, MA, United States
Yang, Wu, Plainsboro, NJ, United States
PATENT ASSIGNEE(S): ARIAD Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6187757	B1	20010213
APPLICATION INFO.:	US 1998-12097		19980122 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-791044, filed on 28 Jan 1997 Continuation-in-part of Ser. No. US 1995-481941, filed on 7 Jun 1995, now abandoned Continuation-in-part of Ser. No. WO 1996-US9948, filed on 7 Jun 1996
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schwartzman, Robert A.
LEGAL REPRESENTATIVE: Berstein, David L.
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 5678
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Materials and methods are disclosed for regulation of biological events such as target gene transcription and growth, proliferation or differentiation of engineered cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 13 OF 59 PCTFULL COPYRIGHT 2002 UniventioDUPLICATE 4
ACCESSION NUMBER: 2001098507 PCTFULL ED 20020826
TITLE (ENGLISH): CHIMERIC HSF TRANSCRIPTION FACTORS
TITLE (FRENCH): FACTEURS DE TRANSCRIPTION HSF CHIMERES
INVENTOR(S): NATESAN, Sridaran; GILMAN, Michael, Z.
PATENT ASSIGNEE(S): ARIAD GENE THERAPEUTICS, INC.; NATESAN, Sridaran; GILMAN, Michael, Z.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2001098507	A1	20011227
DESIGNATED STATES	AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU AT BE CH CY DE DK ES		

FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 2000-US16621 A 20000616
ABEN This invention provides novel materials and methods involving the heterologous expression of transcription factors which are useful for effecting transcription of target genes in genetically engineered cells or organisms containing them. Target gene constructs and other materials useful for practicing the invention are also disclosed.
ABFR La presente invention concerne de nouveaux materiels et de nouvelles methodes faisant intervenir l'expression heterologue de facteurs de transcription qui sont utiles pour la transcription de genes cibles dans les cellules et organismes genetiquement modifies qui les contiennent. L'invention concerne egalement des genes chimeres cibles et autres materiels servant a mettre en oeuvre l'invention.

L12 ANSWER 14 OF 59 USPATFULL
ACCESSION NUMBER: 2001:220852 USPATFULL
TITLE: Chimeric DNA-binding proteins
INVENTOR(S): Pomerantz, Joel L., Cambridge, MA, United States
Sharp, Phillip A., Newton, MA, United States
Pabo, Carl O., Newton, MA, United States
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6326166	B1	20011204	
	WO 9620951		19960711	
APPLICATION INFO.:	US 1998-973131		19980316	(8)
	WO 1995-US16982		19951229	
			19980316	PCT 371 date
			19980316	PCT 102(e) date

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Martinell, James
LEGAL REPRESENTATIVE: Vincent, Matthew P.Ropes & Gray, LLP
NUMBER OF CLAIMS: 60
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 2890
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Chineric proteins containing composite DNA-binding regions are disclosed together with DNA constructs encoding them, compositions containing them and applications in which they are useful.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 15 OF 59 USPATFULL
ACCESSION NUMBER: 2001:29697 USPATFULL
TITLE: ETS2 repressor factor (ERF)
INVENTOR(S): Mavrothalassitis, George J., Frederick, MD, United States
Blair, Donald G., Kensington, MD, United States
Fisher, Robert J., Sharpsburg, MD, United States
Beal, Jr., Gregory J., New Market, MD, United States
Athanasiou, Meropi A., Frederick, MD, United States
Sgouras, Dionyssios N., Athens, Greece
PATENT ASSIGNEE(S): The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6194547	B1	20010227	
APPLICATION INFO.:	US 1998-21715		19980210	(9)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-469412, filed on 5 Jun 1995, now patented, Pat. No. US 5856125
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Pak, Michael
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2381
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates, inter alia, to the ERF gene and to the products encoded by this gene. More particularly, the present invention relates to DNA sequences encoding ERF and AERF; polypeptides encoded by such DNA sequences; ERF chimeric molecules; and methods of using ERF and ERF chimeric molecules to reduce tumorigenicity in a tumor cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 16 OF 59 PCTFULL COPYRIGHT 2002 Univentio
ACCESSION NUMBER: 2001098506 PCTFULL ED 20020826
TITLE (ENGLISH): METHODS AND MEANS FOR REGULATION OF GENE EXPRESSION
TITLE (FRENCH): METHODES ET MOYENS DE REGULATION DE L'EXPRESSION GENIQUE
INVENTOR(S): TONIATTI, Carlo; CILIBERTO, Gennaro; CORTESE, Riccardo
PATENT ASSIGNEE(S): ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ANGELETTI S.P.A; TONIATTI, Carlo; CILIBERTO, Gennaro; CORTESE, Riccardo
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2001098506	A2	20011227
DESIGNATED STATES	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2001-EP6792	A	20010615
PRIORITY INFO.:	GB 2000-0015119.1		20000620

ABEN A **transcription factor**, which is a transcriptional activator or a transcriptional repressor, comprising a DNA-binding domain and a transcriptional activator or repressor domain, and optionally a regulatory domain for ligand-dependent DNA binding and/or transcriptional activation or repression by the **transcription factor**, wherein the **transcription factor** is **chimeric**, comprising a HNF1 polypeptide DNA-binding domain and a transcriptional activator or repressor domain of a different polypeptide, with the proviso that where the **transcription factor** is a transcriptional activator comprising a transcriptional activator domain the **transcription factor** does not comprise a regulatory domain which binds AcylHSL or an analogue thereof whereby upon AcylHSL binding DNA binding function of the DNA-binding domain is activated. A transcriptional activator comprises a human HNF1 polypeptide DNA-binding domain, a human estrogen receptor alpha regulatory domain containing a G521R mutation, and a human **p65** activation domain.

ABFR La presente invention concerne un facteur de transcription, qui est soit un activateur transcriptionnel soit un represseur transcriptionnel, contenant un domaine de liaison d'ADN et un activateur transcriptionnel ou un domaine represseur, et eventuellement un domaine regulateur pour

la liaison d'ADN dependante du ligand et/ou de l'activation ou la repression transcriptionnelle par le facteur transcriptionnel. Le facteur transcriptionnel est un facteur chimere qui comporte un domaine de liaison d'ADN polypeptidique HNF1 et un activateur transcriptionnel ou un domaine represseur d'un autre polypeptide, a condition que lorsque le facteur de transcription est un activateur transcriptionnel comprenant un domaine d'activateur transcriptionnel, le facteur de transcription ne comprend pas de domaine regulateur qui se lie a AcylHSL, ou a un analogue de celui-ci; la fonction de liaison d'ADN liant AcylHSL du domaine de liaison d'ADN etant alors activee. Par ailleurs, un activateur transcriptionnel comprend un domaine de liaison d'ADN polypeptidique HNF1 humain, un domaine regulateur alpha du recepteur d'oestrogenes humain presentant une mutation G521R, et un domaine d'activation p65 humain.

L12 ANSWER 17 OF 59 PCTFULL COPYRIGHT 2002 Univentio
ACCESSION NUMBER: 2001090151 PCTFULL ED 20020826
TITLE (ENGLISH): HUMAN RECEPTOR PROTEINS; RELATED REAGENTS AND METHODS
TITLE (FRENCH): PROTEINES RECEPTRICES HUMAINES, REACTIFS ET METHODES ASSOCIES
INVENTOR(S): HARDIMAN, Gerard, T.; ROCK, Fernando, L.; BAZAN, J., Fernando; KASTELEIN, Robert, A.; HO, Stephen, W. K.; LIU, Yong-Jun
PATENT ASSIGNEE(S): SCHERING CORPORATION
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2001090151	A2	20011129

DESIGNATED STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX MZ NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA UZ VN YU ZA GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 2001-US16766	A	20010523
PRIORITY INFO.:	US 2000-60/207,558		20000525

ABEN Nucleic acids encoding mammalian, e.g., human receptors, purified receptor proteins and fragments thereof. Antibodies, both polyclonal and monoclonal, are also provided. Methods of using the compositions for both diagnostic and therapeutic utilities are provided.

ABFR L'invention concerne des acides nucleiques codant des recepteurs mammaliens, par exemple humains, des proteines receptrices purifiees et leurs fragments. L'invention concerne egalement des anticorps, polyclonaux et monoclonaux, ainsi que des methodes d'utilisation de ces compositions a des fins diagnostiques et therapeutiques.

L12 ANSWER 18 OF 59 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001476046 MEDLINE
DOCUMENT NUMBER: 21412294 PubMed ID: 11521190
TITLE: NF-kappaB/RelA transactivation is required for atypical protein kinase C iota-mediated cell survival.
AUTHOR: Lu Y; Jamieson L; Brasier A R; Fields A P
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Medical Branch, 301 University Blvd., Galveston, Texas, TX 77555-1060, USA.
CONTRACT NUMBER: AI40218 (NIAID)
CA56869 (NCI)
ES06676 (NIEHS)
SOURCE: ONCOGENE, (2001 Aug 9) 20 (35) 4777-92.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20020420
Entered Medline: 20010906

AB In chronic myelogenous leukemia (CML), the oncogene bcr-abl encodes a dysregulated tyrosine kinase that inhibits apoptosis. We showed previously that human erythroleukemia K562 cells are resistant to antineoplastic drug (taxol)-induced apoptosis through the atypical protein kinase C iota isozyme (PKC iota), a kinase downstream of Bcr-Abl. The mechanism(s) by which PKC iota mediates cell survival to taxol is unknown. Here we demonstrate that PKC iota requires the **transcription factor** nuclear **factor**-kappaB (NF-kappaB) to confer cell survival. At apoptosis-inducing concentrations, taxol weakly induces IkappaB(alpha) proteolysis and NF-kappaB translocation in K562 cells, but potently induces its transcriptional activity. Inhibition of NF-kappaB activity (by blocking IkappaB(alpha) degradation) significantly sensitizes cells to taxol-induced apoptosis. Likewise, K562 cells expressing antisense PKC iota mRNA or kinase dead PKC iota (PKC iota-KD) are sensitized to taxol; these cells are rescued from apoptosis by NF-kappaB overexpression. Expression of constitutively active PKC iota (PKC iota-CA) upregulates NF-kappaB transactivation and rescues cells from apoptosis in the absence of Bcr-Abl tyrosine kinase activity. Using a **chimeric** GAL4-**RelA** transactivator, we find that taxol potently activates GAL4-**RelA**-dependent **transcription**. This activation was further upregulated by expression of PKC iota-CA and inhibited by expression of PKC iota-KD. Our results indicate that **RelA** transactivation is an important downstream target of the PKC iota-mediated Bcr-Abl signaling pathway and is required for resistance to taxol-induced apoptosis.

L12 ANSWER 19 OF 59 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:851842 SCISEARCH
THE GENUINE ARTICLE: 478BH
TITLE: Differential regulation of myocardial NF kappa B following acute or chronic TNF-alpha exposure
AUTHOR: Haudek S B; Bryant D D; Giroir B P (Reprint)
CORPORATE SOURCE: Childrens Med Ctr, 1935 Motor St, Dallas, TX 75235 USA (Reprint); Univ Texas, SW Med Ctr, Dept Pediat, Dallas, TX 75390 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MOLECULAR AND CELLULAR CARDIOLOGY, (JUN 2001) Vol. 33, No. 6, pp. 1263-1271.
Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.
ISSN: 0022-2828.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tumor necrosis **factor** alpha (TNF-alpha) is a critical mediator of myocardial dysfunction during acute inflammatory states. TNF-alpha is also present in the serum of patients with chronic cardiac diseases. In monocytes, TNF-alpha stimulates cells by activating distinct signaling pathways that involve nuclear translocation of NF-kappaB. Since NF kappaB may also regulate the expression of genes that could contribute to myocardial dysfunction, the cardiomyocyte NF kappaB activation following acute or chronic TNF-alpha challenges was investigated. To accomplish this, the authors either acutely administered TNF-alpha. to healthy mice, or used transgenic mice which chronically overexpress TNF-alpha exclusively in cardiac myocytes. Following acute administration of TNF-alpha, cardiac NF kappaB translocation was detected from 15 min to

2 h post-challenge. The time course of I kappaB alpha degradation was consistent with the kinetics of NF kappaB translocation. I kappaB beta degradation was slower and less dramatic. In transgenic mice chronically overexpressing TNF-alpha, myocardial NF kappaB activation was detected at all ages tested (21, 40, and 75 days). In contrast to acutely challenged animals, two distinct NF kappaB proteins were activated in chronically challenged animals, p50-**p65** heterodimers as well as p50 homodimers. Activation of both could be transiently blocked by administration of a recombinant **chimeric** TNF-alpha receptor antagonist (rhTNTR:Fc). I kappaB alpha, but not I kappaB beta, levels were elevated in transgenics when compared to wild-type animals. These data indicate that following acute TNF-alpha administration, which simulates bacterial sepsis, myocardial p50-**p65** translocates within minutes. Chronic TNF-alpha exposure, which is thought to occur in long-standing congestive heart failure, results in translocation of transcriptionally inactive p50 homodimers in addition to **transcription** ally active p50-**p65** heterodimers. It is speculated that activation of p50 homodimers constitutes an adaptive response to minimize the inflammatory consequences of chronic cardiac TNT-alpha exposure. (C) 2001 Academic Press.

L12 ANSWER 20 OF 59 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001193318 MEDLINE
DOCUMENT NUMBER: 21106389 PubMed ID: 11158329
TITLE: Glucocorticoid repression of AP-1 is not mediated by competition for nuclear coactivators.
AUTHOR: De Bosscher K; Vanden Berghe W; Haegeman G
CORPORATE SOURCE: Department of Molecular Biology, University of Gent-VIB, K.L. Ledeganckstraat 35, 9000 Gent, Belgium.
SOURCE: MOLECULAR ENDOCRINOLOGY, (2001 Feb) 15 (2) 219-27. Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

AB Interleukin-6 (IL-6) is a pleiotropic cytokine that is involved in many autoimmune and inflammatory diseases. Transcriptional control of IL-6 gene expression is exerted by various compounds, among which glucocorticoids are the most potent antiinflammatory and immunosuppressive agents currently in use. Glucocorticoids exert their transrepressive actions by negatively interfering with **transcription factors**, such as nuclear **factor**-kappaB (NF-kappaB) and AP-1. Both **factors** make use of the coactivator cAMP response element-binding protein (CREB)-binding protein (CBP) to enhance their transcriptional activities, which led to the hypothesis that a mutual antagonism between **p65** or c-Jun and activated glucocorticoid receptor (GR) results from a limited amount of CBP. Recently, we showed that glucocorticoid repression of NF-kappaB-driven gene expression occurs irrespective of the amount of coactivator levels in the cell. In the current study, we extend this observation and demonstrate that also AP-1-targeted gene repression by glucocorticoids is refractory to increased amounts of nuclear coactivators. From results with Gal4 **chimeric** proteins we conclude that glucocorticoid repression occurs by a promoter-independent mechanism involving a nuclear interplay between activated GR and AP-1, independently of CBP levels in the cell.

L12 ANSWER 21 OF 59 USPATFULL DUPLICATE 7
ACCESSION NUMBER: 2000:7210 USPATFULL
TITLE: Transcriptional activators, and compositions and uses related thereto

INVENTOR(S): Natesan, Sridaran, Chestnut Hill, MA, United States
PATENT ASSIGNEE(S): ARIAD Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6015709		20000118
APPLICATION INFO.:	US 1997-920610		19970827 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-918401, filed on 26 Aug 1997, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Degen, Nancy
ASSISTANT EXAMINER: Schwartzman, Robert
LEGAL REPRESENTATIVE: Berstein, David L., Hausdorff, Sharon F., Vincent, Matthew P.
NUMBER OF CLAIMS: 44
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 20 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 3739
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to chimeric transcriptional activators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 22 OF 59 USPATFULL
ACCESSION NUMBER: 2000:174349 USPATFULL
TITLE: Chemical modification of DNA using peptide nucleic acid conjugates
INVENTOR(S): Felgner, Philip L., Rancho Santa Fe, CA, United States
Zelphati, Olivier, La Jolla, CA, United States
Bennett, C. Frank, Carlsbad, CA, United States
PATENT ASSIGNEE(S): Gene Therapy Systems, San Diego, CA, United States (U.S. corporation)
Isis Pharmaceuticals, Inc., Carlsbad, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6165720		20001226
APPLICATION INFO.:	US 1998-224818		19981230 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-87815, filed on 29 May 1998, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-59215P	19970918 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schwartzman, Robert A.
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear LLP
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1773
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Complexes comprising a nucleic acid molecule and a conjugated peptide nucleic acid (PNA). The PNA may be labeled or conjugated to a protein, peptide, carbohydrate moiety or receptor ligand. These complexes are used to transfect cells to monitoring plasmid biodistribution, promote nuclear localization, induce transcriptional activation, lyse the endosomal compartment and facilitate transfection. These complexes increase the efficiency of expression of a particular gene.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 23 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:911419 CAPLUS
DOCUMENT NUMBER: 134:81738
TITLE: Chimeric OCA-B transcription factors for activation of transcription of target genes in a ligand-dependent manner
INVENTOR(S): Natesan, Sridaran
PATENT ASSIGNEE(S): Ariad Gene Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078951	A1	20001228	WO 2000-US16620	20000616
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1194544	A1	20020410	EP 2000-941478	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-140289P P 19990618
WO 2000-US16620 W 20000616

AB This invention provides novel materials and methods involving the heterologous expression of transcription factors which are useful for effecting transcription of target genes in genetically engineered cells or organisms contg. them. These transcription factors are fusion proteins of the B cell-specific transcriptional coactivator OCA-B and a ligand binding domain that can activate transcription of a target gene in a ligand-dependent manner. Target gene constructs and other materials useful for practicing the invention are also disclosed.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 24 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:368623 CAPLUS
DOCUMENT NUMBER: 133:13448
TITLE: Adenovirus vector for gene therapy with modified steroid hormone receptor proteins for target gene expression regulation
INVENTOR(S): Burcin, Mark M.; O'Malley, Bert W.; Schiedner, Gudrun; Tsai, Sophia Y.; Kochanek, Stefan
PATENT ASSIGNEE(S): Valentis, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031286	A1	20000602	WO 1999-US26802	19991112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-109185P P 19981120

AB Adenovirus vector for gene therapy with modified steroid hormone receptor proteins as regulator for therapeutic target gene expression regulation are described. To regulate expression of a transferred gene in response to an exogenous compd., a high capacity adenoviral vector devoid of all viral coding sequences with a regulator gene to control a target gene expression in vivo in a selected site and at a desired time are constructed. The regulator GLp65 (a chimeric transactivator) consists of a mutated progesterone receptor-ligand binding domain fused to the GAL4 DNA binding domain and part of the activation domain of the human p65 protein, a component of the NF-.kappa.B complex. In the presence of ligand RU486, GLp65 binds to a target gene (hGH) contg. the 17-mer GAL4 binding site, resulting in an efficient ligand-inducible transactivation of the target gene. Adenoviral vectors with regulator gene and target gene with or without the insulator sequence (2xHS4, a 5' element of the chicken .beta.-globin domain) are also constructed and tested in animal cells or in transgenic mice. The kinetics of induction and effects of insulator sequence on traget gene are studied. Such vectors are capable of achieving high levels and durations of delivery and expression. The modified regulator protein is capable of distinguishing a hormone agonist from an antagonist and may be modified in the ligand binding domain, the DNA binding domain, and/or the trans-regulatory domain. These regulable adenoviral vectors can be used for potentially diverse applications, ranging from tissue-specific gene expression in transgenic animals to human gene therapy.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 25 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:54166 CAPLUS
DOCUMENT NUMBER: 132:103734
TITLE: Expression systems containing chimeric transactivators which regulate effector gene transcription and their use for manufacture of drugs
INVENTOR(S): Mueller, Rolf; Nettelbeck, Dirk; Sedlacek, Hans-Harald
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland G.m.b.H., Germany
SOURCE: Ger. Offen., 52 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19831420	A1	20000120	DE 1998-19831420	19980714
WO 2000004178	A1	20000127	WO 1999-EP4527	19990701
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9951557	A1	20000207	AU 1999-51557	19990701
BR 9912090	A	20010410	BR 1999-12090	19990701

EP 1097232 A1 20010509 EP 1999-936465 19990701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: DE 1998-19831420 A 19980714
WO 1999-EP4527 W 19990701

AB An expression construct is disclosed which contains component a: .gtoreq.1 promoter; component b: DNA encoding .gtoreq.1 chimeric transactivator which activates transcription from component a and contains DNA coding for a binding domain and DNA coding for a Gln-Ser-Thr-rich transactivation domain; component c: .gtoreq.1 DNA sequence for binding the expression product of component b; component d: .gtoreq.1 minimal promoter contg. the CDE-CHR element of the cdc25 gene or the E2F-BS-CHR element of the cyclin A gene, the 5'-terminus of which is fused to the 3'-terminus of component c; and component e: .gtoreq.1 effector gene, the transcription of which is activated by binding of the component b expression product to component c. Also disclosed are vectors contg. these expression constructs, cells contg. these vectors, and use of these expression constructs and cells to produce pharmaceuticals. Thus, an endothelial cell expression system was prepd. comprising, from 5' to 3', an Sv40 promoter and enhancer, the dog .beta.-globin intron II, the cDNA for the Gal4 binding domain, the cDNA for the transactivation domain of NF-YA, and the SV40 poly(A) signal. A reporter plasmid contg. 5X or 3X GalR binding site, the basal promoter of cdc25 or of the cyclin A gene, and the cDNA for luciferase was used to analyze gene expression in bovine aortic endothelial cells. A higher level of luciferase activity was obsd. in proliferating as opposed to G1-arrested cells.

L12 ANSWER 26 OF 59 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2001091353 MEDLINE
DOCUMENT NUMBER: 20553215 PubMed ID: 11101508
TITLE: The anti-apoptotic activities of Rel and RelA required during B-cell maturation involve the regulation of Bcl-2 expression.
AUTHOR: Grossmann M; O'Reilly L A; Gugasyan R; Strasser A; Adams J M; Gerondakis S
CORPORATE SOURCE: The Walter and Eliza Hall Institute of Medical Research, Post Office, The Royal Melbourne Hospital, Victoria 3050, Australia.
SOURCE: EMBO JOURNAL, (2000 Dec 1) 19 (23) 6351-60.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010125

AB Rel and **RelA**, individually dispensable for lymphopoiesis, serve unique functions in activated B and T cells. Here their combined roles in lymphocyte development were examined in **chimeric** mice repopulated with c-rel(-/-) **rela**(-/-) fetal liver hemopoietic stem cells. Mice engrafted with double-mutant cells lacked mature IgM(lo)IgD(hi) B cells, and numbers of peripheral CD4(+) and CD8(+) T cells were markedly reduced. The absence of mature B cells was associated with impaired survival that coincided with reduced expression of bcl-2 and A1. bcl-2 transgene expression not only prevented apoptosis and increased peripheral B-cell numbers, but also induced further maturation to an IgM(lo)IgD(hi) phenotype. In contrast, the survival of double-mutant T cells was normal and the bcl-2 transgene could not rectify the peripheral T-cell deficit. These findings indicate that Rel and **RelA** serve essential, albeit redundant, functions during the later antigen-independent stages of B- and T-cell maturation, with these **transcription factors** promoting the survival of

peripheral B cells in part by upregulating Bcl-2.

L12 ANSWER 27 OF 59 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2000457778 MEDLINE
DOCUMENT NUMBER: 20424242 PubMed ID: 10969841
TITLE: Endothelin 1 transcription is controlled by nuclear factor-kappaB in AGE-stimulated cultured endothelial cells.
AUTHOR: Quehenberger P; Bierhaus A; Fasching P; Muellner C; Klevesath M; Hong M; Stier G; Sattler M; Schleicher E; Speiser W; Nawroth P P
CORPORATE SOURCE: Department of Medical and Chemical Laboratory Diagnostics, University of Vienna, Austria.
SOURCE: DIABETES, (2000 Sep) 49 (9) 1561-70.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925

AB Incubation of bovine aortic endothelial cells (BAECs) with erythrocytes from patients with type 2 diabetes induced an increase in endothelin 1 (ET-1) production. The effect of erythrocytes on ET-1 synthesis was dependent on glycemic control. ET-1 levels after incubation with erythrocytes derived from patients with HbA(1c) levels <6% were just half the levels observed after incubation with erythrocytes from patients with HbA(1c) levels >8%. Nepsilon-(carboxymethyl)lysine (CML)-containing protein isolated from patients' erythrocytes induced ET-1, and CML-containing protein-dependent ET-1 induction was blocked by the recombinant decoy peptide soluble receptor for advanced glycation end products (AGEs), which comprises the NH2-terminal Ig domain of the receptor for AGEs. In vitro-generated AGEs induced ET-1 mRNA **transcription** (nuclear run-on assay and Northern blot) in a time- and dose-dependent manner. Transient transfection of BAECs with a **chimeric** construct containing the 5' promoter region of the ET-1 gene linked to a reporter gene confirmed that AGE induced ET-1 promoter activity. Electrophoretic mobility shift assay confirmed AGE-inducible binding of members of the nuclear **factor**-kappab (NF-kappaB) family to a potential binding site at -2,090 bp. Binding was functionally significant because overexpression of the cytoplasmic inhibitor of NF-kappaB or deletion of the NF-kappaB binding site reduced ET-1 induction, whereas overexpression of NF-kappaB **p65** induced ET-1 even in the absence of AGEs. Thus, ET-1 **transcription** is controlled by the AGE-inducible redox-sensitive **transcription factor** NF-kappaB.

L12 ANSWER 28 OF 59 USPATFULL
ACCESSION NUMBER: 1999:116975 USPATFULL
TITLE: Methods and compounds for prevention of graft rejection
INVENTOR(S): Strom, Terry, Brookline, MA, United States
Libermann, Towia, Newton, MA, United States
PATENT ASSIGNEE(S): Beth Israel Hospital Association, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5958403		19990928
APPLICATION INFO.:	US 1994-273402		19940711 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-24569, filed on 1 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-843731, filed on 28 Feb 1992, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Stanton, Brian R.
ASSISTANT EXAMINER: Hauda, Karen M.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 30 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2143
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a method of localized immunosuppression which may be used for preventing graft rejection or for preventing tissue destruction due to autoimmune disease. Also disclosed is a protein suppressor factor that is secreted by cloned anergic T-cells, blocks interleukin 2 (IL-2) stimulated T-cell proliferation, has an apparent molecular weight of between 10 and 30 kilodaltons, can be inactivated by heating to 65.degree. C. for 15 minute, blocks interleukin 4 (IL-4) stimulated T-cell proliferation in vitro, is non-cytotoxic to T-cells, and does not inhibit the production of IL-2 by T-cells in vitro.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 29 OF 59 USPATFULL
ACCESSION NUMBER: 1999:1464 USPATFULL
TITLE: ETS2 repressor factor (ERF) genetic locus and its products
INVENTOR(S): Mavrothalassitis, George J., Frederick, MD, United States
Blair, Donald G., Kensington, MD, United States
Fisher, Robert J., Sharpsburg, MD, United States
Beal, Jr., Gregory J., New Market, MD, United States
Athanasiou, Meropi A., Frederick, MD, United States
Sgouras, Dionyssios N., Athens, Greece
PATENT ASSIGNEE(S): The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5856125		19990105	
APPLICATION INFO.:	US 1995-469412		19950605	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Pak, Michael D.
LEGAL REPRESENTATIVE: Townsend & Townsend & Crew LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2799
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates, inter alia, to the ERF gene and to the products encoded by this gene. More particularly, the present invention relates to DNA sequences encoding ERF and AERF; polypeptides encoded by such DNA sequences; ERF chimeric molecules; and methods of using ERF and ERF chimeric molecules to reduce tumorigenicity in a tumor cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 30 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:736960 CAPLUS
DOCUMENT NUMBER: 131:347504
TITLE: Improved multiviral compositions, and uses thereof for inducing rapamycin-dependent transcription of

erythropoietin or growth hormone genes in mammals
INVENTOR(S): Wilson, James; Rivera, Victor; Gilman, Michael; Ye, Xuehai
PATENT ASSIGNEE(S): Ariad Gene Therapeutics, Inc., USA; University of Pennsylvania
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958700	A1	19991118	WO 1999-US10096	19990510
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1078096	A1	20010228	EP 1999-922872	19990510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-76369 A 19980511
WO 1999-US10096 W 19990510

AB The invention provides a method for rendering a mammal capable of rapamycin-dependent transcription of an erythropoietin or growth hormone gene. The method involves infecting the mammal with two different recombinant viruses (adenoviruses, adeno-assocd. viruses, or hybrids thereof). One virus comprises an erythropoietin or growth factor gene operably linked to an IL-2 expression control sequence comprising twelve ZFHD1 binding sites. The other virus contains a bicistronic sequence encoding a ZFHD1-3/FKBP12 DNA-binding fusion protein and an FRB T2098L/p65 transcription activation fusion protein. Expression of erythropoietin or growth factor is induced within the transfected mammal by the administration of rapamycin.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 31 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:767971 CAPLUS
DOCUMENT NUMBER: 132:103653
TITLE: A general strategy to enhance the potency of chimeric transcriptional activators
AUTHOR(S): Natesan, Sridaran; Molinari, Elizabeth; Rivera, Victor M.; Rickles, Richard J.; Gilman, Michael
CORPORATE SOURCE: ARIAD Gene Therapeutics Incorporated, Cambridge, MA, 02139, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(24), 13898-13903
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Efforts to increase the potency of transcriptional activators are generally unsuccessful because poor expression of activators in mammalian cells limits their delivery to target promoters. Here we report that the effectiveness of chimeric activators can be dramatically improved by expressing them as noncovalent tetrameric bundles. Bundled activation domains are much more effective at activating a reporter gene than simple monomeric activators, presumably because, at similar expression levels, up to 4 times as many the activation domains are delivered to the target promoter. These bundled activation domains are also more effective than proteins in which activation domains are tandemly reiterated in the same polypeptide chain, because such proteins are very poorly expressed and therefore not delivered effectively. These observations suggest that

there is a threshold no. of activation domains that must be bound to a promoter for activation, above which promoter activity is simply a function of the no. of activators bound. We show that bundling can be exploited practically to enhance the sensitivity of mammalian two-hybrid assays, enabling detection of weak interactions or those between poorly expressed proteins. Bundling also dramatically improves the performance of a small-mol.-regulated gene expression system when the expression level of regulatory protein is limiting, a situation that may be encountered in gene therapy applications.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 32 OF 59 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1999240736 MEDLINE
DOCUMENT NUMBER: 99240736 PubMed ID: 10224109
TITLE: Immunosuppressant PG490 (triptolide) inhibits T-cell interleukin-2 expression at the level of purine-box/nuclear factor of activated T-cells and NF-kappaB transcriptional activation.
AUTHOR: Qiu D; Zhao G; Aoki Y; Shi L; Uyei A; Nazarian S; Ng J C; Kao P N
CORPORATE SOURCE: Pulmonary and Critical Care Medicine, Stanford University Medical Center, Stanford, California 94305-5236, USA.
CONTRACT NUMBER: K04-01147 (NIAID)
RO1-AI39624
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 May 7) 274 (19) 13443-50.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990614
Last Updated on STN: 19990614
Entered Medline: 19990603

AB PG490 (triptolide) is a diterpene triepoxide with potent immunosuppressive and antiinflammatory properties. PG490 inhibits interleukin(IL)-2 expression by normal human peripheral blood lymphocytes stimulated with phorbol 12-myristate 13-acetate (PMA) and antibody to CD3 (IC50 of 10 ng/ml), and with PMA and ionomycin (Iono, IC50 of 40 ng/ml). In Jurkat T-cells, PG490 inhibits PMA/Iono-stimulated IL-2 **transcription**. PG490 inhibits the induction of DNA binding activity at the purine-box/antigen receptor response element (ARRE)/nuclear **factor** of activated T-cells (NF-AT) target sequence but not at the NF-kappaB site. PG490 can completely inhibit transcriptional activation at the purine-box/ARRE/NF-AT and NF-kappaB target DNA sequences triggered by all stimuli examined (PMA, PMA/Iono, tumor necrosis **factor**-alpha). PG490 also inhibits PMA-stimulated activation of a **chimeric transcription factor** in which the C-terminal TA1 transactivation domain of NF-kappaB **p65** is fused to the DNA binding domain of GAL4. In 16HBE human bronchial epithelial cells, IL-8 expression is regulated predominantly by NF-kappaB, and PG490 but not cyclosporin A can completely inhibit expression of IL-8. The mechanism of PG490 inhibition of cytokine gene expression differs from cyclosporin A and involves nuclear inhibition of transcriptional activation of NF-kappaB and the purine-box regulator operating at the ARRE/NF-AT site at a step after specific DNA binding.

L12 ANSWER 33 OF 59 MEDLINE
ACCESSION NUMBER: 2000038557 MEDLINE
DOCUMENT NUMBER: 20038557 PubMed ID: 10572418
TITLE: Present states of development in new drugs and treatment of inflammatory bowel disease.

AUTHOR: Asakura H; Sugimura K
CORPORATE SOURCE: Third Department of Internal Medicine, School of Medicine, Niigata University.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1999 Nov) 57 (11) 2490-5. Ref: 13
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000127

AB With recent elucidation of pathophysiology and inflammatory process on inflammatory bowel disease(IBD), new drugs and treatments for IBD have developed rapidly. In addition to it, mechanisms of salicylazosulfapyridine, 5-aminosalicylic acid, and glucocorticoid have been clarified at molecular levels as cell **transcription factors** of NF-kappa B. This paper described the following recent therapy performed in IBD patients; 1)leukocytapheresis by G-column, LCAP and centrifugal separator. 2)cytokine and anti-cytokine therapy with anti-TNF-alpha **chimeric** monoclonal antibody and IL-10 for treatment of Crohn' disease. 3)therapy with antisense oligonucleotide against ICAM-1 in Crohn's disease, and against **p65** subunit of NF-kappa B in TNBS induced colitis in mice. 4)therapy modulating receptor function of target cells. 5)therapy with antibody against cell adhesion molecules. 6)radical scavenger therapy with lipo-SOD. And, 7)treatment with low molecular heparin.

L12 ANSWER 34 OF 59 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 2000029301 MEDLINE
DOCUMENT NUMBER: 20029301 PubMed ID: 10565571
TITLE: Inhibition of IL-6 in mice by anti-NF-kappaB oligodeoxyribonucleotide N3'-->oligodeoxyribonnucleotide N3' --> P5' phosphoramidates.
AUTHOR: Wang L; Gryaznov S; Nerenberg M
CORPORATE SOURCE: Medical Biology Institute, Hayward, California 94545, USA.
CONTRACT NUMBER: CA71 143 (NCI)
SOURCE: INFLAMMATION, (1999 Dec) 23 (6) 583-90.
Journal code: 7600105. ISSN: 0360-3997.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991130

AB Oligonucleotide N3'->P5' Phosphoramidates (PN) may confer advantages over unmodified phosphodiester compounds for therapeutic applications (1). Previous in vitro data demonstrated that PN Oligodeoxynucleotides (ODNs) possess several advantageous features, including RNase H-independence, an improved resistance to nuclease degradation, decreased protein binding, and high affinity sequence-specific binding to complementary RNAs (1, 2). Consequently, we undertook a study to investigate the effects of PN antisense (AS) oligos targeted against the **p65** subunit of the Nuclear **Factor** Kappa beta (NF-kappaB) **transcription factor** in vivo, in mice. The ability of the antisense molecules to inhibit IL-6 elevation induced by lipopolysaccharide (LPS) in mice, was studied. A 16 mer uniformly modified PN and a **chimeric** phosphoramidate-phosphodiester oligodeoxynucleotide complementary to the

region surrounding the starting codon, (PN-PO-PN) of the NK-kappaB **p65** subunit mRNA, both caused a sequence specific reduction of the serum IL-6 level in mice. A scrambled oligodeoxynucleotide showed much lower IL-6 inhibition in mice. These results show that the **p65** PN-AS can modulate expression of IL-6 in mice without uptake enhancers and therefore may be a useful prototype for RNAse-H independent therapeutic agents.

L12 ANSWER 35 OF 59 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:63424 CAPLUS
DOCUMENT NUMBER: 130:262805
TITLE: Adenovirus-mediated regulable target gene expression in vivo
AUTHOR(S): Burcin, Mark M.; Schiedner, Gudrun; Kochanek, Stefan; Tsai, Sophia Y.; O'Malley, Bert W.
CORPORATE SOURCE: Department of Cell Biology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(2), 355-360
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To regulate expression of a transferred gene in response to an exogenous compd., we have combined a high capacity adenoviral vector devoid of all viral coding sequences with a regulatory system that can be used to express a target gene in vivo in a selected site and at a desired time. This system uses a chimeric transactivator, GLp65, which consists of a mutated progesterone receptor-ligand binding domain fused to the GAL4 DNA binding domain and part of the activation domain of the human p65 protein, a component of the NF-.kappa.B complex. In the presence of the antiprogestin mifepristone, this chimeric regulator binds to a target gene contg. the 17-mer GAL4 binding site, resulting in an efficient ligand-inducible transactivation of the target gene. We inserted the regulator GLp65 and a regulable human growth hormone target gene contg. the 17-mer GAL4 binding site into the same adenoviral vector. To obtain tissue-specific expression of the target gene, we coupled the regulator to a liver-specific promoter. Infection of HepG2 cells and exptl. mice with the adenovirus resulted in consistently high induction levels of human growth hormone in the presence of mifepristone whereas the transgene expression was undetectable in the absence of the ligand. Taken together, our regulable adenoviral vector represents an important tool for transgene regulation that can be used for potentially diverse applications, ranging from tissue-specific gene expression in transgenic animals to human gene therapy.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 36 OF 59 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1999186585 MEDLINE
DOCUMENT NUMBER: 99186585 PubMed ID: 10088724
TITLE: Regulatory domain of human heat shock transcription factor-2 is not regulated by hemin or heat shock.
AUTHOR: Zhu Z; Mivechi N F
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Department of Radiology, Medical College of Georgia, Augusta 30912, USA.
CONTRACT NUMBER: CA62130 (NCI)
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (1999 Apr 1) 73 (1) 56-69.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990527

AB Heat shock **transcription factor** 2 (HSF-2) activates **transcription** of heat shock proteins in response to hemin in the human erythroleukemia cell line, K562. To understand the regulation of HSF-2 activation, a series of deletion mutants of HSF-2 fused to the GAL-4 DNA binding domain were generated. We have found that **human HSF**-2 has a regulatory domain located in the carboxyl-terminal portion of the protein which represses the activity of its activation domain under normal physiological conditions. The repressive effects of this domain can be eliminated by its deletion in GAL4-HSF-2 fusion constructs. The regulatory domain of HSF-2 can also repress a heterologous **chimeric** activator that contains a portion of the VP16 activation domain. The activation domain of HSF-2 is a segment of approximately 77 amino acids located proximal to the carboxyl-terminal hydrophobic heptad repeat (leucine zipper 4) of the molecule. Interestingly, the GAL4-HSF-2 fusion protein and the 77 amino acids activation domain are inactive and are not activated by pretreatment of cells with either hemin or elevated temperature. Our data suggest that regulation of HSF-2 differs from HSF-1 in that its regulatory domain is not responsive to hemin or heat directly.

L12 ANSWER 37 OF 59 USPATFULL
ACCESSION NUMBER: 1998:45052 USPATFULL
TITLE: Bax promoter sequence and screening assays for indentifying agents that regulate bax gene expression
INVENTOR(S): Reed, John C., Rancho Santa Fe, CA, United States
PATENT ASSIGNEE(S): The Burnham Institute, La Jolla, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5744310		19980428	
APPLICATION INFO.:	US 1996-688145		19960729	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Degen, Nancy
ASSISTANT EXAMINER: Sandals, William
LEGAL REPRESENTATIVE: Campbell & Flores LLP
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 1938
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a substantially purified bax promoter and a nucleic acid molecule containing a nucleotide sequence encoding a gene product operably linked to a bax promoter. The invention also provides a substantially purified active fragment of a bax promoter and a nucleic acid molecule containing a nucleotide sequence encoding a gene product operably linked to an active fragment of a bax promoter. Cell-based screening assays for identifying an effective agent such as a drug that regulates the level of expression of a gene operably linked to a bax promoter, or an active fragment thereof, also are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 38 OF 59 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 1998411354 MEDLINE
DOCUMENT NUMBER: 98411354 PubMed ID: 9738016
TITLE: Heat shock factor 1 mediates hemin-induced hsp70 gene transcription in K562 erythroleukemia cells.
AUTHOR: Yoshima T; Yura T; Yanagi H
CORPORATE SOURCE: HSP Research Institute, Kyoto Research Park, Shimogyo-ku,

Kyoto 600-8813, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 25) 273 (39) 25466-71.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981021
Last Updated on STN: 19981021
Entered Medline: 19981015

AB Transcriptional induction of the hsp70 gene is mediated by **heat shock factor** 1 (HSF1) rapidly activated upon heat and other stresses. HSF2 has been thought to be responsible for accumulation of HSP70 during hemin-induced differentiation of human K562 erythroleukemia cells because of accompanying acquisition of HSF2 DNA binding activity. However, there has not been any direct evidence for such a functional role of HSF2. The purpose of this study is to clarify the roles of HSF1 and HSF2 in HSP70 induction in hemin-treated K562 cells. We show here that a **chimeric** polypeptide of HSF2 and GAL4 DNA binding domain (GAL4-BD-HSF2) was unable to induce a GAL4 binding site-containing luciferase reporter gene in response to hemin and that exogenously overproduced HSF2 also failed to increase expression of a heat shock element-containing reporter. On the contrary, expression of a GAL4-BD-HSF1 **chimeric** protein responded to hemin treatment as well as to heat shock, and transiently overexpressed HSF1 caused hemin-responsive induction of the reporter gene in a dose-dependent manner. These results indicate that HSF1, rather than HSF2, primarily mediates the hemin-induced **transcription** of the hsp70 gene.

L12 ANSWER 39 OF 59 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 1998136163 MEDLINE
DOCUMENT NUMBER: 98136163 PubMed ID: 9468519
TITLE: Role of activating protein-1 in the regulation of the vascular cell adhesion molecule-1 gene expression by tumor necrosis factor-alpha.
AUTHOR: Ahmad M; Theofanidis P; Medford R M
CORPORATE SOURCE: Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia 30322, USA.. mahmad@emory.edu
CONTRACT NUMBER: PO1-HL48667 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Feb 20) 273 (8) 4616-21.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980326
Last Updated on STN: 19980326
Entered Medline: 19980319

AB Endothelial cell surface expression of VCAM-1 is one of the initial steps in the pathogenesis of atherosclerosis. The inflammatory response **transcription factor** nuclear **factor** (NF)-kappaB plays an important role in the regulation of VCAM-1 expression by various stimuli including tumor necrosis **factor** (TNF)-alpha. Other **transcription factors** may modulate this response through interaction with NF-kappaB **factors**. Since c-Fos/c-Jun (activating protein-1 (AP-1)) are expressed in vascular endothelium during proinflammatory conditions, we investigated the role of AP-1 proteins in the expression of VCAM-1 by TNF-alpha in SV40 immortalized human microvascular endothelial cells (HMEC). TNF-alpha induced expression of

both early protooncogenes, c-fos and c-jun. The ability of TNF-alpha to activate the kappaB-motif (kappaL-kappaR)-dependent VCAM-1 promoter-chloramphenicol acetyltransferase (CAT) reporter gene lacking a consensus AP-1 element was markedly inhibited by co-transfection of the expression vector encoding c-fos ribozyme, which decreases the level of c-fos by degrading c-fos mRNA, or c-fos or c-jun oligonucleotides. Conversely, co-transfection of c-Fos and c-Jun encoding expression vectors potentiated the **p65**/NF-kappaB-mediated transactivation of the VCAM-1 promoter-CAT reporter gene. Furthermore the c-Fos encoding expression vector potentiated by 2-fold the transactivation activity of a **chimeric** transcriptional **factor** Gal/**p65** (containing the transactivation domain of **p65** and the DNA binding domain of the yeast transcriptional **factor** Gal-4). Consistent with the promoter studies, curcumin and NDGA, inhibitors of AP-1 activation, markedly inhibited the ability of TNF-alpha to activate the expression of VCAM-1 mRNA levels at concentrations that did not inhibit the activation of NF-kappaB. In gel mobility supershift assays, the antibodies to c-Fos or c-Jun inhibited the binding of TNF-alpha-activated nuclear NF-kappaB to the kappaL-kappaR, suggesting that both c-Fos and c-Jun interacted with NF-kappaB. These results suggest that AP-1 proteins may mediate the effect of TNF-alpha in the regulation of VCAM-1 expression through interaction with NF-kappaB **factors** in endothelial cells.

L12 ANSWER 40 OF 59 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 1998198454 MEDLINE
DOCUMENT NUMBER: 98198454 PubMed ID: 9531535
TITLE: A requirement for NF-kappaB activation in Bcr-Abl-mediated transformation.
AUTHOR: Reuther J Y; Reuther G W; Cortez D; Pendergast A M; Baldwin A S Jr
CORPORATE SOURCE: Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599 USA.
CONTRACT NUMBER: CA61033 (NCI)
CA72771 (NCI)
SOURCE: GENES AND DEVELOPMENT, (1998 Apr 1) 12 (7) 968-81.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980507

AB Bcr-Abl is a **chimeric** oncoprotein that is strongly implicated in acute lymphoblastic (ALL) and chronic myelogenous leukemias (CML). This deregulated tyrosine kinase selectively causes hematopoietic disorders resembling human leukemias in animal models and transforms fibroblasts and hematopoietic cells in culture. Bcr-Abl also protects cells from death induced on cytokine deprivation or exposure to DNA damaging agents. In addition, the antiapoptotic function of Bcr-Abl is thought to play a necessary role in hematopoietic transformation and potentially in leukemogenesis. The **transcription factor** NF-kappaB has been identified recently as an inhibitor of apoptosis and as a potential regulator of cellular transformation. This study shows that expression of Bcr-Abl leads to activation of NF-kappaB-dependent **transcription** by causing nuclear translocation of NF-kappaB as well as by increasing the transactivation function of the **RelA**/**p65** subunit of NF-kappaB. Importantly, this activation is dependent on the tyrosine kinase activity of Bcr-Abl and partially requires Ras. The ability of Bcr-Abl to protect cytokine-dependent 32D myeloid cells from death induced by cytokine deprivation or DNA damage does not, however, require

functional NF-kappaB. However, using a super-repressor form of IkappaBalpha, we show that NF-kappaB is required for Bcr-Abl-mediated tumorigenicity in nude mice and for transformation of primary bone marrow cells. This study implicates NF-kappaB as an important component of Bcr-Abl signaling. NF-kappaB-regulated genes, therefore, likely play a role in transformation by Bcr-Abl and thus in Bcr-Abl-associated human leukemias.

L12 ANSWER 41 OF 59 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 1998078668 MEDLINE
DOCUMENT NUMBER: 98078668 PubMed ID: 9418859
TITLE: Transforming growth factor beta stimulates the human immunodeficiency virus 1 enhancer and requires NF-kappaB activity.
AUTHOR: Li J M; Shen X; Hu P P; Wang X F
CORPORATE SOURCE: Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, North Carolina 27708, USA.
CONTRACT NUMBER: DK45746 (NIDDK)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1998 Jan) 18 (1) 110-21. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980130
Last Updated on STN: 19980130
Entered Medline: 19980122

AB Transforming growth **factor** beta (TGF-beta) is the prototype of a large superfamily of signaling molecules involved in the regulation of cell growth and differentiation. In certain patients infected with human immunodeficiency virus type 1 (HIV-1), increased levels of TGF-beta promoted the production of virus and also impaired the host immune system. In an effort to understand the signaling events linking TGF-beta action and HIV production, we show here that TGF-beta can stimulate **transcription** from the HIV-1 long terminal repeat (LTR) promoter through NF-kappaB binding sites in both HaCaT and 300.19 pre-B cells. When introduced into a minimal promoter, NF-kappaB binding sites supported nearly 30-fold activation from the luciferase reporter upon TGF-beta treatment. Electrophoretic mobility shift assay indicated that a major **factor** binding to the NF-kappaB site is the p50-**p65** heterodimeric NF-kappaB in HaCaT cells. Coexpression of Gal4-**p65** **chimeric** proteins supported TGF-beta ligand-dependent gene expression from a luciferase reporter gene driven by Gal4 DNA binding sites. NF-kappaB activity present in HaCaT cells was not affected by TGF-beta treatment as judged by the unchanged DNA binding activity and concentrations of p50 and **p65** proteins. Consistently, steady-state levels of IkappaB alpha and IkappaB beta proteins were not changed by TGF-beta treatment. Our results demonstrate that TGF-beta is able to stimulate **transcription** from the HIV-1 LTR promoter by activating NF-kappaB through a mechanism distinct from the classic NF-kappaB activation mechanism involving the degradation of IkappaB proteins.

L12 ANSWER 42 OF 59 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 1998101759 MEDLINE
DOCUMENT NUMBER: 98101759 PubMed ID: 9440809
TITLE: Cross-talk between nuclear factor-kappa B and the steroid hormone receptors: mechanisms of mutual antagonism.
AUTHOR: McKay L I; Cidlowski J A
CORPORATE SOURCE: National Institutes of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina 27709, USA.

SOURCE: MOLECULAR ENDOCRINOLOGY, (1998 Jan) 12 (1) 45-56.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980218

AB Nuclear **factor** kappa B (NF-kappa B) is an inducible **transcription factor** that positively regulates the expression of proimmune and proinflammatory genes, while glucocorticoids are potent suppressors of immune and inflammatory responses. NF-kappa B and the glucocorticoid receptor (GR) physically interact, resulting in repression of NF-kappa B transactivation. In transient cotransfection experiments, we demonstrate a dose-dependent, mutual antagonism between NF-kappa B and GR. Functional dissection of the NF-kappa B p50 and **p65** subunits and deletion mutants of GR indicate that the GR antagonism is specific to the **p65** subunit of NF-kappa B heterodimer, whereas multiple domains of GR are essential to repress **p65**-mediated transactivation. Despite its repression of GR transactivation, **p65** failed to block the transrepressive GR homologous down-regulation function. We also demonstrate that negative interactions between **p65** and GR are not selective for GR, but also occur between NF-kappa B and androgen, progesterone B, and estrogen receptors. However, although each of these members of the steroid hormone receptor family is repressed by NF-kappa B, only GR effectively inhibits **p65** transactivation. Further, in cotransfections using a **chimeric** estrogen-GR, the presence of the GR DNA-binding domain is insufficient to confer mutual antagonism to the **p65**-estrogen receptor interaction. Selectivity of **p65** repression for each steroid receptor is demonstrated by I kappa B rescue from NF-kappa B-mediated inhibition. Together these data suggest that NF-kappa B **p65** physically interacts with multiple steroid hormone receptors, and this interaction is sufficient to transrepress each steroid receptor. Further, the NF-kappa B status of a cell has the potential to significantly alter multiple steroid signaling pathways within that cell.

L12 ANSWER 43 OF 59 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 97407940 MEDLINE
DOCUMENT NUMBER: 97407940 PubMed ID: 9261164
TITLE: A new function for the C-terminal zinc finger of the glucocorticoid receptor. Repression of RelA transactivation.
AUTHOR: Liden J; Delaunay F; Rafter I; Gustafsson J; Okret S
CORPORATE SOURCE: Department of Medical Nutrition, Karolinska Institute, Huddinge University Hospital, Novum F60, S-141 86 Huddinge, Sweden.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Aug 22) 272 (34) 21467-72.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970926
Last Updated on STN: 20000303
Entered Medline: 19970915

AB Glucocorticoids inhibit NF-kappaB signaling by interfering with the NF-kappaB **transcription factor RelA**.
Previous studies have identified the DNA-binding domain (DBD) in the glucocorticoid receptor (GR) as the major region responsible for this

repressive activity. Using GR mutants with **chimeric** DBDs the repressive function was found to be located in the C-terminal zinc finger. As predicted from these results the mineralocorticoid receptor that contains a C-terminal zinc finger identical to that of the GR was also able to repress **RelA**-dependent **transcription**. Mutation of a conserved arginine or a lysine in the second zinc finger of the GR DBD (Arg-488 or Lys-490 in the rat GR) abolished the ability of GR to inhibit **RelA** activity. In contrast, C-terminal zinc finger GR mutants with mutations in the dimerization box or mutations necessary for full transcriptional GR activity were still able to repress **RelA** -dependent **transcription**. In addition, we found that the steroid analog ZK98299 known to induce GR transrepression of AP-1 had no inhibitory effect on **RelA** activity. In summary, these results demonstrate that the inhibition of NF-kappaB by glucocorticoids involves two critical amino acids in the C-terminal zinc finger of the GR. Furthermore, the results from the use of mineralocorticoid receptor and anti-glucocorticoids suggest that the mechanisms for GR-mediated repression of NF-kappaB and AP-1 are different.

L12 ANSWER 44 OF 59 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 1998208264 MEDLINE
DOCUMENT NUMBER: 98208264 PubMed ID: 9548485
TITLE: Role of cyclic AMP response element-binding protein in cyclic AMP inhibition of NF-kappaB-mediated transcription.
AUTHOR: Parry G C; Mackman N
CORPORATE SOURCE: Department of Immunology, The Scripps Research Institute, La Jolla, CA 92037, USA.
CONTRACT NUMBER: HL-48872 (NHLBI)
HL-56609 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1997 Dec 1) 159 (11) 5450-6.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980430
Last Updated on STN: 19980430
Entered Medline: 19980420

AB The NF-kappaB family of **transcription factors** regulates the inducible expression of a variety of genes. Recently, we showed that elevation of intracellular cyclic AMP inhibits NF-kappaB-mediated **transcription** in human monocytes and endothelial cells without preventing nuclear translocation of NF-kappaB complexes. The present study examined the molecular mechanism of this inhibition. We hypothesized that activation of the protein kinase A signaling pathway may inhibit NF-kappaB-mediated **transcription** by phosphorylating proteins, such as cAMP response element-binding protein (CREB), which compete for limiting amounts of the coactivator CBP. Here, we show that the amino-terminal region (amino acids 1-450) of CBP specifically interacts with the carboxyl-terminal region (amino acids 286-551) of NF-kappaB **p65** (**RelA**) both in vitro and in vivo. Functional studies using human endothelial cells demonstrated that overexpression of CBP rescued cAMP inhibition of NF-kappaB-mediated **transcription** and **transcription** mediated by a **chimeric** protein, GAL4-**p65**(286-551), which contained the GAL4 DNA binding domain fused to the carboxyl-terminal region of **p65** (amino acids 286-551). In contrast, overexpression of CREB inhibited GAL4-**p65**(286-551)-mediated **transcription**. These results suggest that activation of the protein kinase A pathway inhibits NF-kappaB **transcription** by phosphorylating CREB, which competes with **p65** for limiting amounts of CBP.

L12 ANSWER 45 OF 59 MEDLINE DUPLICATE 20

ACCESSION NUMBER: 1998028695 MEDLINE
DOCUMENT NUMBER: 98028695 PubMed ID: 9359875
TITLE: HSF1 granules: a novel stress-induced nuclear compartment of human cells.
AUTHOR: Cotto J; Fox S; Morimoto R
CORPORATE SOURCE: Department of Biochemistry, Rice Institute for Biomedical Research, Northwestern University, Evanston, IL 60208, USA.
SOURCE: JOURNAL OF CELL SCIENCE, (1997 Dec) 110 (Pt 23) 2925-34. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19990129
Entered Medline: 19980205

AB **Heat shock factor** 1 (HSF1) is the ubiquitous stress-responsive transcriptional activator which is essential for the inducible **transcription** of genes encoding heat shock proteins and molecular chaperones. HSF1 localizes within the nucleus of cells exposed to heat shock, heavy metals, and amino acid analogues, to form large, irregularly shaped, brightly staining granules which are not detected during attenuation of the heat shock response or when cells are returned to their normal growth conditions. The kinetics of detection of HSF1 granules parallels the transient induction of heat shock gene **transcription**. HSF1 granules are also detected using an HSF1-Flag epitope tagged protein or a **chimeric** HSF1-green fluorescent protein which reveals that these nuclear structures are stress-induced and can be detected in living cells. The spatial organization of HSF1 granules in nuclei of stressed cells reveals that they are novel nuclear structures which are stress-dependent and provides evidence that the nucleus undergoes dynamic reorganization in response to stress.

L12 ANSWER 46 OF 59 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 1998054021 MEDLINE
DOCUMENT NUMBER: 98054021 PubMed ID: 9393872
TITLE: Activation of p65 NF-kappaB protein by p210BCR-ABL in a myeloid cell line (P210BCR-ABL activates p65 NF-kappaB).
AUTHOR: Hamdane M; David-Cordonnier M H; D'Halluin J C
CORPORATE SOURCE: INSERM U124, Onco-Hematologie Moleculaire, Institut de Recherches sur le Cancer de Lille, France.
SOURCE: ONCOGENE, (1997 Nov 6) 15 (19) 2267-75. Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971222

AB The **chimeric** tyrosine kinase p210BCR-ABL is involved in the pathogenesis of chronic myelogenous leukemia. It transforms immature hematopoietic cells in vitro and abrogates IL-3-dependent growth. The mechanisms by which p210BCR-ABL mediates its oncogenicity are not well elucidated. Identifying **transcription factors** targeted by the **chimeric** protein may help to clarify these mechanisms. We have analysed the effect of p210BCR-ABL expression on NF-kappaB activity in DA1 cells (an IL-3-dependent murine myeloid progenitor cell line). A specific stimulation of NF-kappaB activity by kinase-active wild-type p210BCR-ABL has been evidenced by transcriptional activation assays. Electrophoretic mobility supershift assays revealed the presence of **p65** protein (**RelA**) DNA binding activity in p210BCR-ABL

transformed DA1 cells but not in parental DA1 cells. Activation of **RelA** in transformed DA1 cells may occur by protein stabilization. Experiments using oligonucleotides antisense to **RelA** showed that p210BCR-ABL transfected cells failed to survive after IL-3 removal. Moreover, inhibition of cellular growth was shown following treatment of p210BCR-ABL transformed DA1 cells by **p65** antisense oligonucleotides. This study suggests that **p65** NF-kappaB may be an effector for p210BCR-ABL and probably contributes to its induced transformation process.

L12 ANSWER 47 OF 59 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 97184457 MEDLINE
DOCUMENT NUMBER: 97184457 PubMed ID: 9032259
TITLE: Rac regulation of transformation, gene expression, and actin organization by multiple, PAK-independent pathways.
AUTHOR: Westwick J K; Lambert Q T; Clark G J; Symons M; Van Aelst L; Pestell R G; Der C J
CORPORATE SOURCE: Department of Pharmacology and Lineberger Comprehensive Cancer Center, University of North Carolina School of Medicine, Chapel Hill, 27599-7038, USA.
CONTRACT NUMBER: CA42978 (NCI)
CA55008 (NCI)
CA63071 (NCI)
+
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1997 Mar) 17 (3) 1324-35.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 20000303
Entered Medline: 19970314

AB Rac1 and RhoA are members of the Rho family of Ras-related proteins and function as regulators of actin cytoskeletal organization, gene expression, and cell cycle progression. Constitutive activation of Rac1 and RhoA causes tumorigenic transformation of NIH 3T3 cells, and their functions may be required for full Ras transformation. The effectors by which Rac1 and RhoA mediate these diverse activities, as well as the interrelationship between these events, remain poorly understood. Rac1 is distinct from RhoA in its ability to bind and activate the **p65** PAK serine/threonine kinase, to induce lamellipodia and membrane ruffling, and to activate the c-Jun NH2-terminal kinase (JNK). To assess the role of PAK in Rac1 function, we identified effector domain mutants of Rac1 and Rac1-RhoA **chimeric** proteins that no longer bound PAK. Surprisingly, PAK binding was dispensable for Rac1-induced transformation and lamellipodium formation, as well as activation of JNK, p38, and serum response **factor** (SRF). However, the ability of Rac1 to bind to and activate PAK correlated with its ability to stimulate **transcription** from the cyclin D1 promoter. Furthermore, Rac1 activation of JNK or SRF, or induction of lamellipodia, was neither necessary nor sufficient for Rac1 transforming activity. Finally, the signaling pathways that mediate Rac1 activation of SRF or JNK were distinct from those that mediate Rac1 induction of lamellipodia. Taken together, these observations suggest that Rac1 regulates at least four distinct effector-mediated functions and that multiple pathways may contribute to Rac1-induced cellular transformation.

L12 ANSWER 48 OF 59 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:438198 BIOSIS
DOCUMENT NUMBER: PREV199699151804
TITLE: Anatomy of TRAF2: Distinct domains for nuclear factor-kappa-B activation and association with tumor

necrosis factor signaling proteins.
AUTHOR(S): Takeuchi, Masahiro; Rothe, Mike; Goeddel, David V. (1)
CORPORATE SOURCE: (1) Tularik Inc., 2 Corporate Dr., South San Francisco, CA 94080 USA
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 33, pp. 19935-19942.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The tumor necrosis **factor** (TNF) receptor-associated **factor** (TRAF) family of proteins interact with and transduce signals for members of the TNF receptor superfamily. TRAF1, TRAF2, and TRAF3 share a conserved C-terminal TRAF domain. TRAF2 plays a key role in transducing signals for activation of the **transcription factor** nuclear **factor**-kappa-B (NF-kappa-B). We have performed extensive mutational analysis on TRAF2, examining the requirements for **NF-KB** activation, self-association, and interaction with other molecules involved in TNF signaling. Examination of point mutants and TRAF2-TRAF3 **chimeric** proteins indicates that the N-terminal RING finger and two adjacent zinc fingers of TRAF2 are required for NF-kappa-CB activation. The two distinct TRAF-N and TRAF-C subdomains of the TRAF domain appear to independently mediate self-association and interaction with TRAF1. Interaction of TRAF2 with TNF-R2 and TRADD requires sequences at the C terminus of the TRAF-C domain, whereas interaction with the protein kinase receptor-interacting protein V(RIP) occurs via sequences at the N terminus of the TRAF-C domain. Thus, distinct domains of TRAF2 are involved in recruitment and signaling functions.

L12 ANSWER 49 OF 59 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 96189106 MEDLINE
DOCUMENT NUMBER: 96189106 PubMed ID: 8628291
TITLE: A glycine-rich region in NF-kappaB p105 functions as a processing signal for the generation of the p50 subunit.
AUTHOR: Lin L; Ghosh S
CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute, New Haven, Connecticut 06520, USA.
CONTRACT NUMBER: R01-AI33443 (NIAID)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 May) 16 (5) 2248-54.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 20000303
Entered Medline: 19960621
AB **Transcription factor** NF-kappaB is generally considered to be a heterodimer with two subunits, p50 and **p65**. The p50 subunit has been suggested to be generated from its precursor, p105, via the ubiquitin-proteasome pathway. During processing, the C-terminal portion of p105 is rapidly degraded whereas the N-terminal portion (p50) is left intact. We report here that a 23-amino-acid, glycine-rich region (GRR) in p105 functions as a processing signal for the generation of p50. A GRR-dependent endoproteolytic cleavage downstream of the GRR releases p50 from p105, and this cleavage does not require any specific downstream sequences. p50 can be generated from **chimeric** precursor p105N-GRR-IkappaBalpha, while the C-terminal portion (IkappaBalpha) can also be recovered, suggesting that p105 processing includes two steps: a GRR-dependent endoproteolytic cleavage and the subsequent degradation of the C-terminal portion. We have also demonstrated that the GRR can direct a similar processing event when it is inserted into a protein unrelated to

the NF-kappaB family and that it is therefore an independent signal for processing.

L12 ANSWER 50 OF 59 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 96182086 MEDLINE
DOCUMENT NUMBER: 96182086 PubMed ID: 8622685
TITLE: The regulatory domain of human heat shock factor 1 is sufficient to sense heat stress.
AUTHOR: Newton E M; Knauf U; Green M; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 Mar) 16 (3) 839-46. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960627
Last Updated on STN: 19960627
Entered Medline: 19960618

AB **Heat shock factor** (HSF) activates **transcription** in response to cellular stress. Human HSF1 has a central regulatory domain which can repress the activity of its activation domains at the control temperature and render them heat shock inducible. To determine whether the regulatory domain works in tandem with specific features of the HSF1 transcriptional activation domains, we first used deletion and point mutagenesis to define these activation domains. One of the activation domains can be reduced to just 20 amino acids. A GAL4 fusion protein containing the HSF 1 regulatory domain and this 20-amino-acid activation domain is repressed at the control temperature but potently activates **transcription** in response to heat shock. No specific amino acids in this activation domain are required for response to the regulatory domain; in particular, none of the potentially phosphorylated serine and threonine residues are required for heat induction, implying that heat-induced phosphorylation of the transcriptional activation domains is not required for induction. The regulatory domain is able to confer heat responsiveness to an otherwise completely heterologous **chimeric** activator that contains a portion of the VP16 activation domain, suggesting that the regulatory domain can sense heat in the absence of other portions of HSF1.

L12 ANSWER 51 OF 59 MEDLINE
ACCESSION NUMBER: 96430529 MEDLINE
DOCUMENT NUMBER: 96430529 PubMed ID: 8833654
TITLE: Angiotensinogen gene activation by angiotensin II is mediated by the rel A (nuclear factor-kappaB p65) transcription factor: one mechanism for the renin angiotensin system positive feedback loop in hepatocytes.
AUTHOR: Li J; Brasier A R
CORPORATE SOURCE: Departments Internal Medicine and Sealy Center for Molecular Science, University of Texas Medical Branch, Galveston, USA.
CONTRACT NUMBER: 1R29-HL-45500 (NHLBI)
SOURCE: MOLECULAR ENDOCRINOLOGY, (1996 Mar) 10 (3) 252-64. Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 20000303

Entered Medline: 19970501

AB The renin-angiotensin system controls blood pressure through the enzymatic production of the vasopressor angiotensin II (AII) from the angiotensinogen (AGT) precursor. Intravascular AII production stimulates de novo synthesis of its precursor in a positive feedback loop through increased gene expression. In this study, we investigate the effects of AII on AGT gene expression. At nanomolar concentrations, All activates **transcription** of the native AGT gene; this region is mapped to the AGT gene multihormone-inducible enhancer (-615 to -470). Within the multihormone-inducible enhancer, site-directed mutations of the acute-phase response element (APRE) that interfere with nuclear **factor**-kappa B (NF-kappa B) **transcription factor** binding also abolish All responsiveness. The APRE functions as a rapidly inducible All-inducible enhancer with peak reporter activity detected after a 4-h stimulation; this effect occurs only when the type 1 AII receptor is expressed. All induces sequence-specific **NF-KB** binding to the APRE in HepG2 nuclear extracts. Moreover, AII infusions of primary rat hepatocyte cultures produces a rapid 4-fold increase in sequence-specific NF-kappa B binding to the APRE. Antibodies against the transcriptional activator subunit, Rel A, quantitatively supershift the nucleoprotein complex, whereas antibodies to other NF-kappa B members do not, demonstrating that Rel A APRE-binding activity is AII-inducible. Transient overexpression of Rel A(1-551) activates the AGT multihormone-inducible enhancer. AII-inducible domains of Rel A were mapped by cotransfecting a **chimeric** GAL4-Rel A fusion protein with a reporter gene containing GAL4-binding sites. GAL4-Rel A(1-551) was an AII-inducible transactivator. Deletion of the NH(2)-terminal 254 amino acids of Rel A produces a constitutive transactivator, indicating that Rel A is activated by AII in a manner dependent on its NH(2) terminus. These studies define one mechanism for the renin-angiotensin system positive feedback loop in hepatocyctes.

L12 ANSWER 52 OF 59 MEDLINE DUPLICATE 25
ACCESSION NUMBER: 96405041 MEDLINE
DOCUMENT NUMBER: 96405041 PubMed ID: 8809181
TITLE: Generation of estrogen receptor mutants with altered ligand specificity for use in establishing a regulatable gene expression system.
AUTHOR: Whelan J; Miller N
CORPORATE SOURCE: Glaxo Institute for Molecular Biology, Plan-Les-Ouates Geneva, Switzerland.
SOURCE: JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1996 Apr) 58 (1) 3-12.
Journal code: 9015483. ISSN: 0960-0760.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19970203
Entered Medline: 19961024

AB Considerable interest exists in developing an artificial system for the control of gene expression, based on the hormone binding domain (HBD) of steroid receptors. In this study we describe a yeast based approach which allows the identification of mutations within the HBD of steroid receptors, in this case the estrogen receptor, which result in altered specificity of the HBD with respect to its activation by ligands. Using this approach in yeast, we identified an estrogen receptor (HBD) mutant (His524 to Gln) whose activation by 17 beta-estradiol (E2) is significantly reduced while activation by a diphenol indene-ol compound (GR132706X) is increased, compared to the wild type estrogen receptor. When the activity of the mutant receptor was tested in mammalian cells the altered specificity was maintained. A **chimeric**

transcription factor was constructed, in which the mutated estrogen receptor HBD was linked to the DNA binding domain of GAL4 and an 11 amino acid transcriptional activation domain of **RelA**. Reporter gene activation by this chimera was decreased in response to E2 and increased in response to GR132706X, as compared to the corresponding **chimeric transcription factor** containing the wild type estrogen receptor HBD. This approach should allow the development of a steroid receptor HBD based regulator of gene expression, whose activity is controlled specifically by a synthetic ligand, that would not affect the activity of endogenous steroid receptors.

L12 ANSWER 53 OF 59 MEDLINE DUPLICATE 26
ACCESSION NUMBER: 96094309 MEDLINE
DOCUMENT NUMBER: 96094309 PubMed ID: 7493948
TITLE: Role of a distal enhancer containing a functional NF-kappa B-binding site in lipopolysaccharide-induced expression of a novel alpha 1-antitrypsin gene.
AUTHOR: Ray A; Gao X; Ray B K
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Missouri, Columbia 65211, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Dec 8) 270 (49) 29201-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L42320
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960111

AB alpha 1-Antitrypsin (alpha 1-AT) is one of the major proteinase inhibitors in serum. Its primary physiological function is to inhibit neutrophil elastase activity in lung, but it also inhibits other serine proteases including trypsin, chymotrypsin, thrombin, and cathepsin. We have previously reported a novel alpha 1-AT, S-2 isoform, from rabbit that is induced up to 100-fold in the liver during acute inflammatory condition (Ray, B. K., Gao, X., and Ray, A. (1994) J. Biol. Chem. 269, 22080-22086). Here, we present evidence that the expression of this alpha 1-AT S-2 gene is also induced in lipopolysaccharide (LPS)-treated peripheral blood monocytes. From the cloned genomic DNA, we have identified a distal LPS-responsive enhancer located between -2438 and -1990 base pairs upstream of the **transcription** start site. In vitro DNA-binding studies demonstrated an interaction of an LPS-inducible NF-kappa B-like nuclear **factor** with a kappa B-element present in this enhancer region. Antibodies against **p65** and p50 subunits of NF-kappa B supershifted the DNA-protein complex. A mutation of the NF-kappa B-binding element virtually abolished the LPS-responsive induction of the **chimeric** promoter in monocytic cells. Furthermore, overexpression of NF-kappa B induced the wild-type promoter activity. Taken together, these results demonstrated that during LPS-mediated inflammation, NF-kappa B/Rel family of **transcription factors** play a crucial role in the transcriptional induction of the inflammation responsive alpha 1-AT gene.

L12 ANSWER 54 OF 59 MEDLINE DUPLICATE 27
ACCESSION NUMBER: 95280936 MEDLINE
DOCUMENT NUMBER: 95280936 PubMed ID: 7760831
TITLE: A heat shock-responsive domain of human HSF1 that regulates transcription activation domain function.
AUTHOR: Green M; Schuetz T J; Sullivan E K; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.

CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1995 Jun) 15 (6) 3354-62.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950707
Last Updated on STN: 19970203
Entered Medline: 19950628

AB **Human heat shock factor** 1 (HSF1) stimulates **transcription** from heat shock protein genes following stress. We have used **chimeric** proteins containing the GAL4 DNA binding domain to identify the transcriptional activation domains of HSF1 and a separate domain that is capable of regulating activation domain function. This regulatory domain conferred heat shock inducibility to **chimeric** proteins containing the activation domains. The regulatory domain is located between the transcriptional activation domains and the DNA binding domain of HSF1 and is conserved between mammalian and chicken HSF1 but is not found in HSF2 or HSF3. The regulatory domain was found to be functionally homologous between chicken and human HSF1. This domain does not affect DNA binding by the **chimeric** proteins and does not contain any of the sequences previously postulated to regulate DNA binding of HSF1. Thus, we suggest that activation of HSF1 by stress in humans is controlled by two regulatory mechanisms that separately confer heat shock-induced DNA binding and transcriptional stimulation.

L12 ANSWER 55 OF 59 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93343857 EMBASE
DOCUMENT NUMBER: 1993343857
TITLE: Heterologous C-terminal sequences disrupt transcriptional activation and oncogenesis by p59(v-rel).
AUTHOR: Diehl J.A.; Hannink M.
CORPORATE SOURCE: Biochemistry Department, University of Missouri,Columbia, MO 65212, United States
SOURCE: Journal of Virology, (1993) 67/12 (7161-7171).
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Members of the **NF-kB**/rel family of **transcription factors** are regulated through a trans association with members of a family inhibitor proteins, collectively known as IkB proteins, that contain five to eight copies of a 33-amino-acid repeat sequence (ankyrin repeat). Certain **NF-kB**/rel proteins are also regulated by cis-acting ankyrin repeat-containing domains. The C terminus of p105(**NF-kB**), the precursor of the 50-kDa subunit of **NF-kB**, contains a series of ankyrin repeats; proteolytic removal of this ankyrin domain is necessary for the manifestation of sequence-specific DNA binding and nuclear translocation of the N-terminal product. To investigate the structural requirements important for regulation of different **NF-kB**/rel family members by polypeptides containing ankyrin repeat domains, we have constructed a p59(v-rel):p105(**NF-kB**) **chimeric** protein (p110(v-rel-ank)). The presence of C-terminal p105(**NF-kB**)-derived sequences in p110(v-rel-ank) inhibited nuclear translocation, sequence-specific DNA binding, PP40(IkB-.alpha.) association, and oncogenic transformation. Sequential truncation of the C- terminal ankyrin domain of p110(v-rel-ank) resulted in the restoration of nuclear translocation, DNA binding, and

pp40(IkB-.alpha.) association but did not restore the oncogenic properties of p59(v-rel). The presence of 67 C-terminal p105(**NF-kB**)-derived amino acids was sufficient to inhibit both transcriptional activation and oncogenic transformation by p59(v-rel). These results support a model in which activation of gene expression by p59(v-rel) is required for its ability to induce oncogenic transformation.

L12 ANSWER 56 OF 59 MEDLINE DUPLICATE 28
ACCESSION NUMBER: 93180814 MEDLINE
DOCUMENT NUMBER: 93180814 PubMed ID: 8441404
TITLE: Conservation of transcriptional activation functions of the NF-kappa B p50 and p65 subunits in mammalian cells and Saccharomyces cerevisiae.
AUTHOR: Moore P A; Ruben S M; Rosen C A
CORPORATE SOURCE: Roche Institute of Molecular Biology, Roche Research Center, Nutley, New Jersey 07110.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1993 Mar) 13 (3) 1666-74.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930416
Last Updated on STN: 19930416
Entered Medline: 19930401

AB The NF-kappa B **transcription factor** complex is composed of a 50-kDa (p50) and a 65-kDa (**p65**) subunit. Both subunits bind to similar DNA motifs and elicit transcriptional activation as either homo- or heterodimers. By using **chimeric** proteins that contain the DNA binding domain of the yeast transcriptional activator GAL4 and subdomains of **p65**, three distinct transcriptional activation domains were identified. One domain was localized to a region of 42 amino acids containing a potential leucin zipper structure, consistent with earlier reports. Two other domains, both acidic and rich in prolines, were also identified. Of perhaps more significance, the same minimal activation domains that were functional in mammalian cells were also functional in the yeast Saccharomyces cerevisiae. Coexpression of the NF-kappa B inhibitory molecule, I kappa B, reduced the transcriptional activity of **p65** significantly, suggesting the ability of I kappa B to function in a similar manner in S. cerevisiae. Surprisingly, while the conserved rel homology domain of **p65** demonstrated no transcriptional activity in either mammalian cells or S. cerevisiae, the corresponding domain in p50 was a strong transcriptional activator in S. cerevisiae. The observation that similar domains elicit transcriptional activation in mammalian cells and S. cerevisiae demonstrates strong conservation of the transcriptional machinery required for NF-kappa B function and provides a powerful genetic system to study the transcriptional mechanisms of these proteins.

L12 ANSWER 57 OF 59 MEDLINE DUPLICATE 29
ACCESSION NUMBER: 93054546 MEDLINE
DOCUMENT NUMBER: 93054546 PubMed ID: 1331059
TITLE: Tumor necrosis factor alpha and interferon gamma synergistically induce interleukin 8 production in a human gastric cancer cell line through acting concurrently on AP-1 and NF-kB-like binding sites of the interleukin 8 gene.
AUTHOR: Yasumoto K; Okamoto S; Mukaida N; Murakami S; Mai M; Matsushima K
CORPORATE SOURCE: Department of Pharmacology, Kanazawa University, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31) 22506-11.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921201

AB Interleukin 8 (IL-8) is a novel cytokine which possesses neutrophil chemotactic and activating activities in addition to chemotactic activity for basophils and T lymphocytes. It has been shown that IL-8 is produced by a variety of human somatic cells including monocytes/macrophages, dermal fibroblasts, vascular endothelial cells, keratinocytes, mesangeal cells, and several types of tumor cell lines. We have examined here whether or not human gastric cancer cell lines produce IL-8 in vitro. The production of IL-8 protein was detected by enzyme-linked immunosorbent assay in the culture supernatants derived from eight of nine human gastric cancer cell lines stimulated with either interleukin 1 alpha (IL-1 alpha), tumor necrosis **factor** alpha (TNF alpha), or TNF alpha plus interferon gamma (IFN gamma). In some of the gastric cancer cell lines such as MKN 45 and KATO, TNF alpha plus IFN gamma synergistically induced the production of IL-8. In MKN 45 cells, synergistic increase of the steady state level of IL-8 mRNA by TNF alpha plus IFN gamma was not inhibited by cycloheximide treatment. Scatchard analysis revealed that IFN gamma changed neither the number nor the affinity constant of TNF alpha binding sites on a gastric cancer cell line, suggesting that the synergism was a post-receptor event. Furthermore, synergistic induction of chloramphenicol acetyltransferase activity by TNF alpha plus IFN gamma was observed in MKN 45 that were transiently transfected with **chimeric** chloramphenicol acetyltransferase reporter genes driven by the transcriptional regulatory region of human IL-8 gene. Through the mutation of the regulatory region of the IL-8 gene, both AP-1- and **NF-kB**-like **factor** binding elements were presumed to be involved in conferring the responsiveness to TNF alpha plus IFN gamma. Moreover, gel retardation analyses revealed that TNF alpha and IFN gamma synergistically induced the binding of **NF-kB** like as well as AP-1 like proteins bound to these sites. These results indicated that IFN gamma synergistically enhanced TNF alpha-induced IL-8 production in a human gastric cancer cell line through synergistic activation of **transcription factors** without up-regulating TNF alpha receptor.

L12 ANSWER 58 OF 59 MEDLINE DUPLICATE 30
ACCESSION NUMBER: 93024383 MEDLINE
DOCUMENT NUMBER: 93024383 PubMed ID: 1406630
TITLE: Selection of optimal kappa B/Rel DNA-binding motifs: interaction of both subunits of NF-kappa B with DNA is required for transcriptional activation.
AUTHOR: Kunsch C; Ruben S M; Rosen C A
CORPORATE SOURCE: Department of Gene Regulation, Roche Institute of Molecular Biology, Nutley, New Jersey 07110.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1992 Oct) 12 (10) 4412-21. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921026

AB Analysis of the p50 and **p65** subunits of the NF-kappa B **transcription factor** complex has revealed that both proteins can interact with related DNA sequences through either homo- or

heterodimer formation. In addition, the product of the proto-oncogene c-rel can bind to similar DNA motifs by itself or as a heterodimer with p50 or **p65**. However, these studies have used a limited number of known kappa B DNA motifs, and the question of the optimal DNA sequences preferred by each homodimer has not been addressed. Using purified recombinant p50, **p65**, and c-Rel proteins, optimal DNA-binding motifs were selected from a pool of random oligonucleotides. Alignment of the selected sequences allowed us to predict a consensus sequence for binding of the individual homodimeric Rel-related proteins, and DNA-protein binding analysis of the selected DNA sequences revealed sequence specificity of the proteins. Contrary to previous assumptions, we observed that **p65** homodimers can interact with a subset of DNA sequences not recognized by p50 homodimers. Differential binding affinities were also obtained with p50- and c-Rel-selected sequences. Using either a p50- or **p65**-selected kappa B motif, which displayed differential binding with respect to the other protein, little to no binding was observed with the heterodimeric NF-kappa B complex. Similarly, in transfection experiments in which the selective kappa B binding sites were used to drive the expression of a chloramphenicol acetyltransferase reporter construct, the **p65**- and p50-selected motifs were activated only in the presence of **p65** and p50/65 (a **chimeric** protein with the p50 DNA binding domain and **p65** activation domain) expression vectors, respectively, and neither demonstrated a significant response to stimuli that induce NF-kappa B activity. These findings demonstrate that interaction of both subunits of the heterodimeric NF-kappa B complex with DNA is required for DNA binding and transcriptional activation and suggest that transcriptional activation mediated by the individual rel-related proteins will differ dramatically, depending on the specific kappa B motifs present.

L12 ANSWER 59 OF 59 MEDLINE DUPLICATE 31
ACCESSION NUMBER: 92123171 MEDLINE
DOCUMENT NUMBER: 92123171 PubMed ID: 1732726
TITLE: Functional characterization of the NF-kappa B p65 transcriptional activator and an alternatively spliced derivative.
AUTHOR: Ruben S M; Narayanan R; Klement J F; Chen C H; Rosen C A
CORPORATE SOURCE: Department of Gene Regulation, Roche Institute of Molecular Biology, Nutley, New Jersey 07110-1199.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1992 Feb) 12 (2) 444-54. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 19920315
Last Updated on STN: 19920315
Entered Medline: 19920224

AB The NF-kappa B **transcription factor** complex is composed of two proteins, designated p50 and **p65**, both having considerable homology to the product of the rel oncogene. We present evidence that the **p65** subunit is a potent transcriptional activator in the apparent absence of the p50 subunit, consistent with in vitro results demonstrating that **p65** can interact with DNA on its own. To identify the minimal activation domain, **chimeric** fusion proteins between the DNA binding domain of the yeast transcriptional activator protein GAL4 and regions of the carboxy terminus of **p65** were constructed, and their transcriptional activity was assessed by using a GAL4 upstream activation sequence-driven promoter-chloramphenicol acetyltransferase fusion. This analysis suggests that the boundaries of the activation domain lie between amino acids 415 and 550. Moreover, single amino acid changes within residues 435 to 459 greatly diminished activation. Similar to other activation domains, this

region contains a leucine zipper-like motif as well as an overall net negative charge. To identify those residues essential for DNA binding, we made use of a naturally occurring derivative of **p65**, lacking residues 222 to 231 (hereafter referred to as **p65** delta), and produced via an alternative splice site. Gel mobility shift analysis using bacterially expressed **p65**, **p65** delta, and various mutants indicates that residues 222 to 231 are important for binding to kappa B DNA. Coimmunoprecipitation analysis suggests that these residues likely contribute to the multimerization function required for homomeric complex formation or heteromeric complex formation with p50 in that no association of **p65** delta with itself or with p50 was evident. However, **p65** delta was able to form weak heteromeric complexes with **p65** that were greatly reduced in their ability to bind DNA. On the basis of these findings, we suggest that subtle changes within the proposed multimerization domain can elicit different effects with the individual Rel-related proteins and that a potential role of **p65** delta may be to negatively regulate NF-kappa B function through formation of nonfunctional heteromeric complexes.

=> d 1-5 ibib abs

L9 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 1999186585 MEDLINE
DOCUMENT NUMBER: 99186585 PubMed ID: 10088724
TITLE: Regulatory domain of human heat shock transcription factor-2 is not regulated by hemin or heat shock.
AUTHOR: Zhu Z; Mivechi N F
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Department of Radiology, Medical College of Georgia, Augusta 30912, USA.
CONTRACT NUMBER: CA62130 (NCI)
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (1999 Apr 1) 73 (1) 56-69.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990527

AB Heat shock **transcription factor** 2 (HSF-2) activates **transcription** of heat shock proteins in response to hemin in the human erythroleukemia cell line, K562. To understand the regulation of HSF-2 activation, a series of deletion mutants of HSF-2 fused to the GAL-4 DNA binding domain were generated. We have found that **human HSF**-2 has a regulatory domain located in the carboxyl-terminal portion of the protein which represses the activity of its activation domain under normal physiological conditions. The repressive effects of this domain can be eliminated by its deletion in GAL4-HSF-2 fusion constructs. The regulatory domain of HSF-2 can also repress a heterologous **chimeric** activator that contains a portion of the VP16 activation domain. The activation domain of HSF-2 is a segment of approximately 77 amino acids located proximal to the carboxyl-terminal hydrophobic heptad repeat (leucine zipper 4) of the molecule. Interestingly, the GAL4-HSF-2 fusion protein and the 77 amino acids activation domain are inactive and are not activated by pretreatment of cells with either hemin or elevated temperature. Our data suggest that regulation of HSF-2 differs from HSF-1 in that its regulatory domain is not responsive to hemin or heat directly.

L9 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 1998411354 MEDLINE
DOCUMENT NUMBER: 98411354 PubMed ID: 9738016
TITLE: Heat shock factor 1 mediates hemin-induced hsp70 gene transcription in K562 erythroleukemia cells.
AUTHOR: Yoshima T; Yura T; Yanagi H
CORPORATE SOURCE: HSP Research Institute, Kyoto Research Park, Shimogyo-ku, Kyoto 600-8813, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 25) 273 (39) 25466-71.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981021
Last Updated on STN: 19981021
Entered Medline: 19981015

AB Transcriptional induction of the hsp70 gene is mediated by **heat shock factor** 1 (HSF1) rapidly activated upon heat and other stresses. HSF2 has been thought to be responsible for accumulation of HSP70 during hemin-induced differentiation of human K562

erythroleukemia cells because of accompanying acquisition of HSF2 DNA binding activity. However, there has not been any direct evidence for such a functional role of HSF2. The purpose of this study is to clarify the roles of HSF1 and HSF2 in HSP70 induction in hemin-treated K562 cells. We show here that a **chimeric** polypeptide of HSF2 and GAL4 DNA binding domain (GAL4-BD-HSF2) was unable to induce a GAL4 binding site-containing luciferase reporter gene in response to hemin and that exogenously overproduced HSF2 also failed to increase expression of a heat shock element-containing reporter. On the contrary, expression of a GAL4-BD-HSF1 **chimeric** protein responded to hemin treatment as well as to heat shock, and transiently overexpressed HSF1 caused hemin-responsive induction of the reporter gene in a dose-dependent manner. These results indicate that HSF1, rather than HSF2, primarily mediates the hemin-induced **transcription** of the hsp70 gene.

L9 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 1998028695 MEDLINE
DOCUMENT NUMBER: 98028695 PubMed ID: 9359875
TITLE: HSF1 granules: a novel stress-induced nuclear compartment of human cells.
AUTHOR: Cotto J; Fox S; Morimoto R
CORPORATE SOURCE: Department of Biochemistry, Rice Institute for Biomedical Research, Northwestern University, Evanston, IL 60208, USA.
SOURCE: JOURNAL OF CELL SCIENCE, (1997 Dec) 110 (Pt 23) 2925-34. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19990129
Entered Medline: 19980205

AB **Heat shock factor** 1 (HSF1) is the ubiquitous stress-responsive transcriptional activator which is essential for the inducible **transcription** of genes encoding heat shock proteins and molecular chaperones. HSF1 localizes within the nucleus of cells exposed to heat shock, heavy metals, and amino acid analogues, to form large, irregularly shaped, brightly staining granules which are not detected during attenuation of the heat shock response or when cells are returned to their normal growth conditions. The kinetics of detection of HSF1 granules parallels the transient induction of heat shock gene **transcription**. HSF1 granules are also detected using an HSF1-Flag epitope tagged protein or a **chimeric** HSF1-green fluorescent protein which reveals that these nuclear structures are stress-induced and can be detected in living cells. The spatial organization of HSF1 granules in nuclei of stressed cells reveals that they are novel nuclear structures which are stress-dependent and provides evidence that the nucleus undergoes dynamic reorganization in response to stress.

L9 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 96182086 MEDLINE
DOCUMENT NUMBER: 96182086 PubMed ID: 8622685
TITLE: The regulatory domain of human heat shock factor 1 is sufficient to sense heat stress.
AUTHOR: Newton E M; Knauf U; Green M; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 Mar) 16 (3) 839-46. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960627
Last Updated on STN: 19960627
Entered Medline: 19960618

AB **Heat shock factor** (HSF) activates **transcription** in response to cellular stress. Human HSF1 has a central regulatory domain which can repress the activity of its activation domains at the control temperature and render them heat shock inducible. To determine whether the regulatory domain works in tandem with specific features of the HSF1 transcriptional activation domains, we first used deletion and point mutagenesis to define these activation domains. One of the activation domains can be reduced to just 20 amino acids. A GAL4 fusion protein containing the HSF 1 regulatory domain and this 20-amino-acid activation domain is repressed at the control temperature but potently activates **transcription** in response to heat shock. No specific amino acids in this activation domain are required for response to the regulatory domain; in particular, none of the potentially phosphorylated serine and threonine residues are required for heat induction, implying that heat-induced phosphorylation of the transcriptional activation domains is not required for induction. The regulatory domain is able to confer heat responsiveness to an otherwise completely heterologous **chimeric** activator that contains a portion of the VP16 activation domain, suggesting that the regulatory domain can sense heat in the absence of other portions of HSF1.

L9 ANSWER 5 OF 5 MEDLINE
ACCESSION NUMBER: 95280936 MEDLINE
DOCUMENT NUMBER: 95280936 PubMed ID: 7760831
TITLE: A heat shock-responsive domain of human HSF1 that regulates transcription activation domain function.
AUTHOR: Green M; Schuetz T J; Sullivan E K; Kingston R E
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: GM43901 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1995 Jun) 15 (6) 3354-62. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950707
Last Updated on STN: 19970203
Entered Medline: 19950628

AB **Human heat shock factor** 1 (HSF1) stimulates **transcription** from heat shock protein genes following stress. We have used **chimeric** proteins containing the GAL4 DNA binding domain to identify the transcriptional activation domains of HSF1 and a separate domain that is capable of regulating activation domain function. This regulatory domain conferred heat shock inducibility to **chimeric** proteins containing the activation domains. The regulatory domain is located between the transcriptional activation domains and the DNA binding domain of HSF1 and is conserved between mammalian and chicken HSF1 but is not found in HSF2 or HSF3. The regulatory domain was found to be functionally homologous between chicken and human HSF1. This domain does not affect DNA binding by the **chimeric** proteins and does not contain any of the sequences previously postulated to regulate DNA binding of HSF1. Thus, we suggest that activation of HSF1 by stress in humans is controlled by two regulatory mechanisms that separately confer heat shock-induced DNA binding and transcriptional stimulation.